DOES NOT CIRCULATE

UNIVERSITY
OF MICHIGAN
OCT 6 - 1955
MEDICAL
LIBRARY

SURGERY

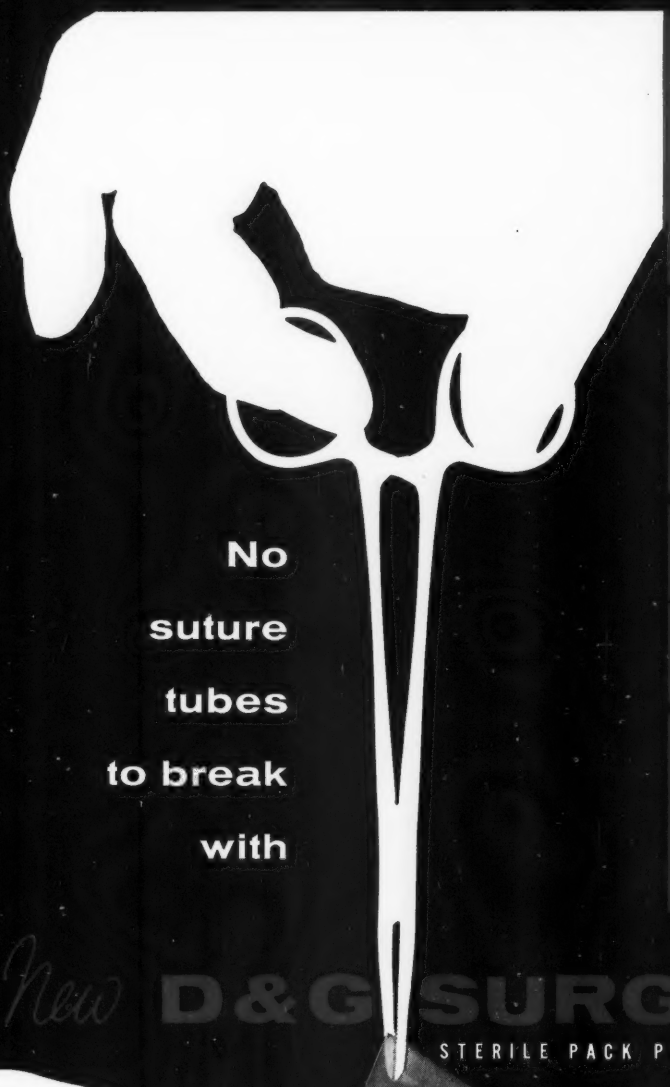
Gynecology & Obstetrics

WITH

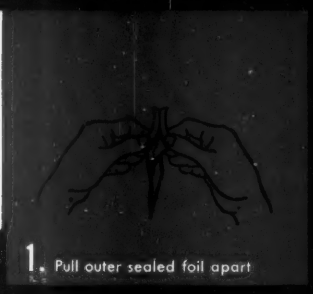
INTERNATIONAL ABSTRACTS OF SURGERY

October, 1955

VOLUME 101 • NUMBER 4

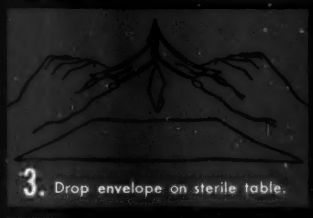


No suture tubes to break with



1. Pull outer sealed foil apart

2. Remove envelope with forceps or . . .

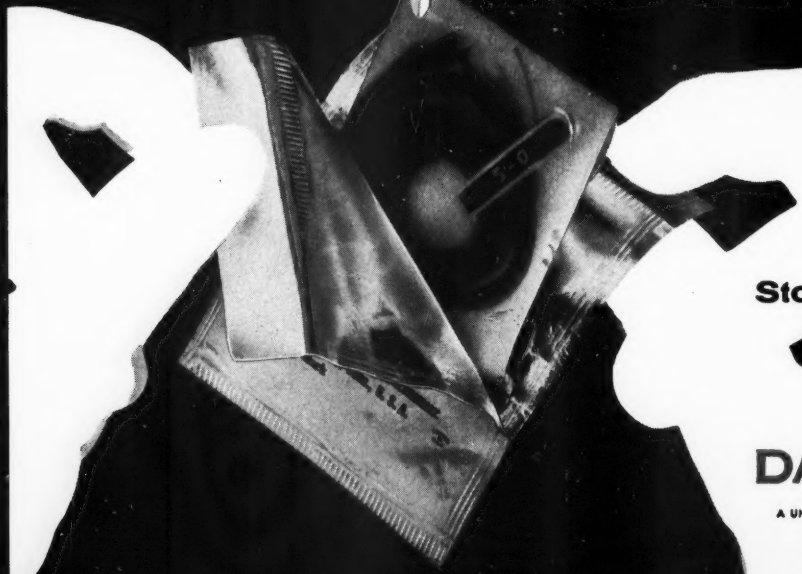


3. Drop envelope on sterile table.

4. Remove pre-cut sutures with tab.

New D&G SURGILOPE*

STERILE PACK PRE-CUT ANACAP SILK



Costs less

Stores in one-third of the space

D&G®

DAVIS & GECK INC.

A UNIT OF AMERICAN Cyanamid COMPANY

DANBURY, CONNECTICUT

*SURGILOPE AND ANACAP ARE D & G TRADEMARKS.

SURGERY

Gynecology & Obstetrics OCTOBER 1955

With International Abstracts of Surgery

OFFICIAL SCIENTIFIC JOURNAL OF THE AMERICAN COLLEGE OF SURGEONS

Editor, LOYAL DAVIS

Associate Editors

SUMNER L. KOCH · MICHAEL L. MASON

JAMES T. PRIESTLEY

Consulting Editors

UNITED STATES AND CANADA

JOEL W. BAKER · JOHN I. BREWER
JAMES BARRETT BROWN · MICHAEL E. DE BAKEY
DANIEL C. ELKIN · FRANK GLENN
WALTER C. MacKENZIE · FRANCIS M. McKEEVER
REED M. NESBIT · NEWELL W. PHILPOTT

GREAT BRITAIN

H. J. B. ATKINS · W. ARTHUR MACKEY
SIR JAMES PATERSON ROSS

ARGENTINA CARLOS A. TANTURI
AUSTRALIA HENRY SEARBY
BRAZIL MOACYR EYCK ALVARO
DENMARK JENS K. FOGED
FRANCE PIERRE MALLET-GUY
NORWAY CARL SEMB
SWEDEN CLARENCE CRAFOORD
URUGUAY PEDRO LARGHERO YBARZ

Published by

THE FRANKLIN H. MARTIN MEMORIAL FOUNDATION

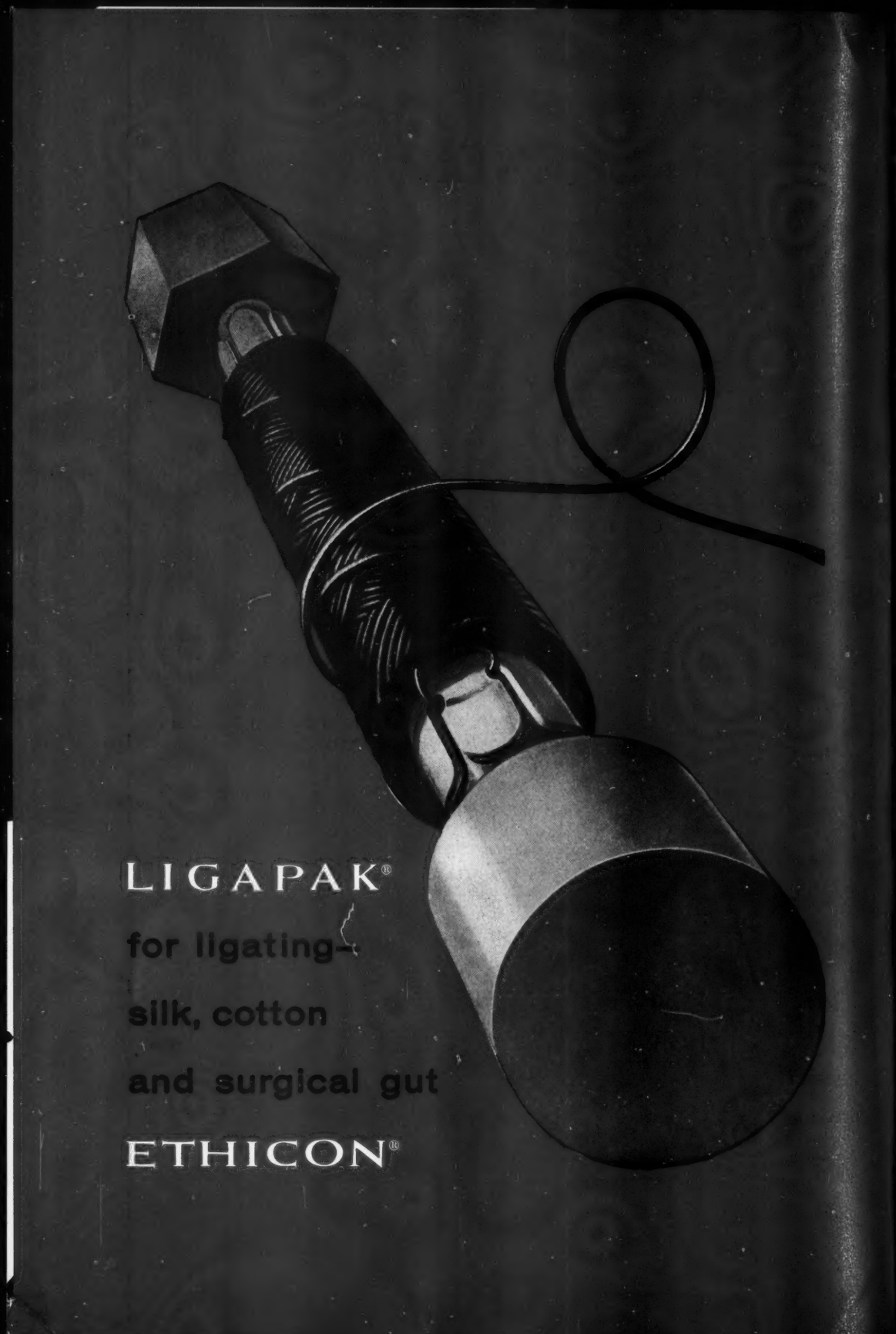
JAMES S. SHANNON, *General Manager*

EDITORIAL AND BUSINESS OFFICES · 54 EAST ERIE STREET, CHICAGO 11, ILLINOIS, U. S. A.

Annual Subscription: United States and Canada, $15.00; Other Countries, $17.00. Published Monthly. Entered as second-class matter January 14, 1931, at the postoffice at Chicago, Ill., under the Act of Congress, March 3, 1879.

Copyright, 1955, by The Franklin H. Martin Memorial Foundation.

London Office: 8 Henrietta Street, Covent Garden, W. C. 2.


LIGAPAK®
for ligating—
silk, cotton
and surgical gut
ETHICON®

SURGERY OCTOBER 1955
Gynecology & Obstetrics VOLUME 101
NUMBER 4

CONTENTS

SUBDIAPHRAGMATIC FUNDUSECTOMY IN GASTRIC SURGERY. *F. Holle* and *G. Heinrich*, Würzburg, Germany 385

THE MANAGEMENT OF CANCER OF THE MAXILLARY ANTRUM. *Donald Raines, M.D.*, and *Arthur G. James, M.D., F.A.C.S.*, Columbus, Ohio 395

A SKIN BANK FOR POSTMORTEM HOMOGRAFTS. *James Barrett Brown, M.D., F.A.C.S., Minot P. Fryer, M.D., F.A.C.S.*, and *Thomas J. Zaydon, M.D.*, St. Louis, Missouri 401

AN ANALYSIS OF PULMONARY RESECTION IN 513 CASES OF TUBERCULOSIS. *F. H. Cole, M.D., F.A.C.S.*, and *F. H. Alley, M.D., F.A.C.S.*, Memphis, Tennessee 413

RUPTURE OF THE STOMACH IN THE NEWBORN INFANT. *Lester L. Vargas, M.D., Sheldon M. Levin, M.D.*, and *Thomas V. Santulli, M.D., F.A.C.S.*, New York, New York 417

BRONCHOGRAPHY WITH DIONOSIL. *G. H. C. Joynt, M.D., F.A.C.S., F.R.C.S. (Can.)*, and *L. R. Harnick, M.D.*, Toronto, Canada 425

BENEFICIAL ACTION OF PRETREATMENT WITH CHLORPROMAZINE ON SURVIVAL FOLLOWING GRADED HEMORRHAGE IN THE RAT. *S. G. Hershey, M.D., I. Guccione, B.S.*, and *B. W. Zweifach, Ph.D.*, New York, New York 431

A STUDY OF 50,000 SPECIMENS OF THE HUMAN VERMIFORM APPENDIX. *Donald C. Collins, M.D., M.S. (Path., Surg.), Sc.D., F.A.C.S.*, Hollywood, California 437

THE RESULTS OF DIRECT VISION CLOSURE OF VENTRICULAR SEPTAL DEFECTS IN EIGHT PATIENTS BY MEANS OF CONTROLLED CROSS CIRCULATION. *C. Walton Lillehei, M.D., F.A.C.S., Morley Cohen, M.D., Herbert E. Warden, M.D., Newell R. Ziegler, M.D.*, and *Richard L. Varco, M.D., F.A.C.S.*, Minneapolis, Minnesota 446

STUDIES OF FIBRINOGEN AND OTHER HEMOSTATIC FACTORS IN WOMEN WITH INTRAUTERINE DEATH AND DELAYED DELIVERY. *Jack A. Pritchard, M.D.*, Dallas, Texas, and *Oscar D. Ratnoff, M.D.*, Cleveland, Ohio 467

[CONTENTS CONTINUED ON PAGE 7]

in hysterosalpingography

ETHIODOL®

(BRAND OF ETHIODIZED OIL)

new LIPIODOL® diagnostic

with

free-flowing viscosity

optimally absorbed

yet permits 24-hour film

Normal hysterosalpingogram with ETHIODOL

Double uterus with single cervix and probable duplication of tubes—demonstrated by hysterosalpingography with ETHIODOL

New, ethiodized oil* for diagnostic x-ray purposes, ETHIODOL is specially formulated to preserve all the benefits of its parent preparation, LIPIODOL, while avoiding the technical disadvantages and excessively rapid absorption of some aqueous media.

free-flowing viscosity
calibrated fluidity for free passage through strictured tubes or narrow ducts.

excellent radiopacity
sharp x-ray films, as with LIPIODOL, for dependable diagnosis.

clinically bland
nontoxic, nonirritating, well tolerated without discomfort.

optimal absorption
permits 24-hour film for more accurate determination of tubal patency.

*ETHIODOL, brand of ethiodized oil, is the ethyl ester of the iodized fatty acids of poppy seed oil, containing 37% iodine. Available in 10 cc. ampules, boxes of two.

For additional scientific information, write to:

FOUGERA

E. FOUGERA & COMPANY, INC.
75 Varick Street, New York 13, N. Y.

Physiologic Alterations with Massive Blood Replacement. *William S. Howland, M.D., Olga Schweizer, M.D., C. Paul Boyan, M.D.*, and *Alma C. Dotto, M.D.*, New York, New York 478

Morbidity of Abdominoperineal Resection. *Joseph A. Buckwalter, M.D., F.A.C.S.*, Iowa City, Iowa, *Richard Shropshire, M.D.*, Great Falls, Montana, and *Bennett A. Joiner, M.D., F.A.C.S.*, San Angelo, Texas 483

Editorials

National Surgical Treatment of Duodenal Ulcer. *Edgar J. Poth, M.D., Ph.D., F.A.C.S.*, Galveston, Texas 489

The Surgeon Retires. *Allen O. Whipple, M.D., F.A.C.S.*, Princeton, New Jersey 492

The Surgeon at Work

Partial Section of Proximal Seventh Nerve Trunk for Facial Spasm. *W. B. Scoville, M.D., F.A.C.S.*, Hartford, Connecticut 494

The Surgeon's Library

James Douglas and the Peritoneal Cul-de-Sac. *Harold Speert, M.D., F.A.C.S.*, New York, New York 498

Review of New Books 502–506

Books Received 506

American College of Surgeons

Preliminary Plans for the 41st Clinical Congress—The Conrad Hilton Hotel, Chicago, Illinois, October 31 to November 4, 1955 507–528

International Abstracts of Surgery

Contents i-viii

Collective Review: American Radiology—1905 to 1955. *Paul G. Swanson, M.D.*, Philadelphia, Pennsylvania 313–325

Abstracts of Important Contributions in the Current Surgical Literature 326–416

SURGERY
Gynecology & Obstetrics
OCTOBER 1955
VOLUME 101
NUMBER 4

SUBDIAPHRAGMATIC FUNDUSECTOMY IN GASTRIC SURGERY

F. HOLLE and G. HEINRICH, Würzburg, Germany

IN GASTRIC SURGERY during recent years, as in many branches of modern surgery, some apparently unshakeable views have changed and new appreciations have come to the fore. Chiefly this has been due to the impulse given by the American surgeons—Lahey, Lewis, Ivor, Brunschwig, Marshall, Sweet, and others—who tackled the problem of the operative treatment of pathologic processes in the cardiac and fundus region of the stomach, and mastered the technique of total gastrectomy with removal of neighboring organs and intrathoracic anastomosis of the esophagus with the upper end of the small intestine. They showed that it was possible for the patient to go on living although his stomach had been completely removed. Although critical voices were raised in the American medical press itself over this extremely mutilating operation and its sequelae by Abrahamson, Allison, Priestley, ReMine, and Ransom, the enthusiasm for this operation and its broadened range of suitable indications extended beyond America to Gütgemann, Lortat-Jacob, Tomoda, Winkelbauer.

From the Department of Surgery, University Hospital, Würzburg.

In carcinoma of the stomach the indication for total gastrectomy was not restricted to those cases in which, as a result of the extension of the pathologic process, no other choice is left (*gastrectomie de nécessité*), but was suggested for every type of carcinoma of the stomach on the grounds of the radical nature of total gastrectomy (*gastrectomie de principe*). A few surgeons (Gütgemann, Tomoda) recommended total resection in certain cases even for ulcers situated high up in the subcardiac region. The more radical group of surgeons believe that by these methods they can improve the 5 year cure rate of gastric carcinoma which has previously stood at a very unsatisfactory figure. Clear cut statistical evidence on this point is lacking, however. The more conservative group of surgeons, therefore, continue to employ the well tried technique of partial resection. They see, for example, in the Billroth II operation and its modifications, a satisfactory compromise which best suits the requirements of general gastric surgery. They undertake total gastrectomies for high situated carcinomas and ulcers only with reluctance, for they fear, not without justification, the high mortality rate, the greater

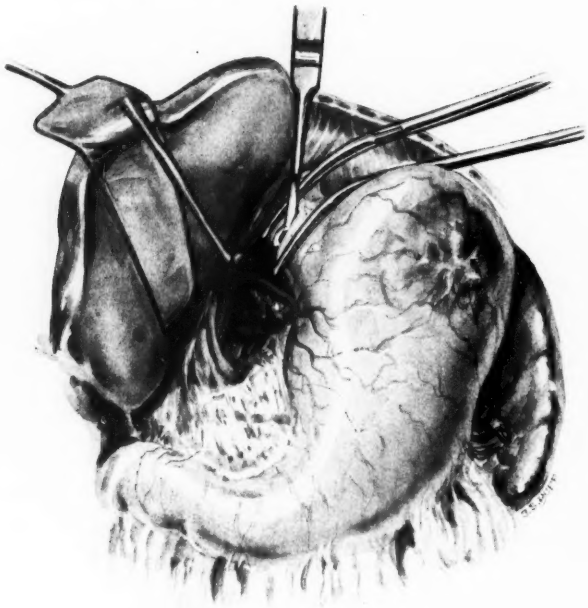


FIG. 1. The cardia is secured, above and below, between two clamps and is transected. The esophageal branches of the gastric artery are held toward the medial line. From the intra-abdominal stump of the esophagus a biopsy specimen is taken.

number of complications, and the high incidence of relapses with which this major intervention is associated. They generally prefer, therefore, the palliative resection in cases of a subcardiac ulcer (Madlener) and gastrostomy in cases of a high carcinoma.

Many years of experience were required before it was shown conclusively that both the enthusiasm of the extreme radical for excision and the rigid and unyielding attitude of the extreme conservative school were capable of leading to error.

Experience of total resection has taught us that this severely mutilating intervention frequently has devastating after-effects. It has now been quite definitely shown that after total resection of the stomach, an imbalance in the metabolism of fat, protein, and carbohydrate occurs. The resulting disorders are often hardly compatible with life. The agastric anemia, which leads within 5 to 6 years to a true pernicious anemia, is another factor against a routine adoption of total gastrectomy.

On the other hand, however, it is known that a gastrostomy cannot prevent the rapid course of advancing cachexia that occurs with a high gastric carcinoma. Also, the palliative type of resection in gastric ulcer cannot exclude the danger of malignant transformation, further hemorrhage, and stenosis. It is, therefore, clear that: (1) the surety of a radical excision by more extreme interventions cannot now be increased by any worthwhile amount, but the number of postoperative complications does increase with the severity of the intervention; (2) no more of the stomach than necessary shall be sacrificed. This applies above all to the prepyloric part of the stomach. Holle and Heinrich, Nissen, and Wachsmuth have pointed out the importance of this section of the stomach for a satisfactory postoperative gastric function; (3) all pathologic processes in

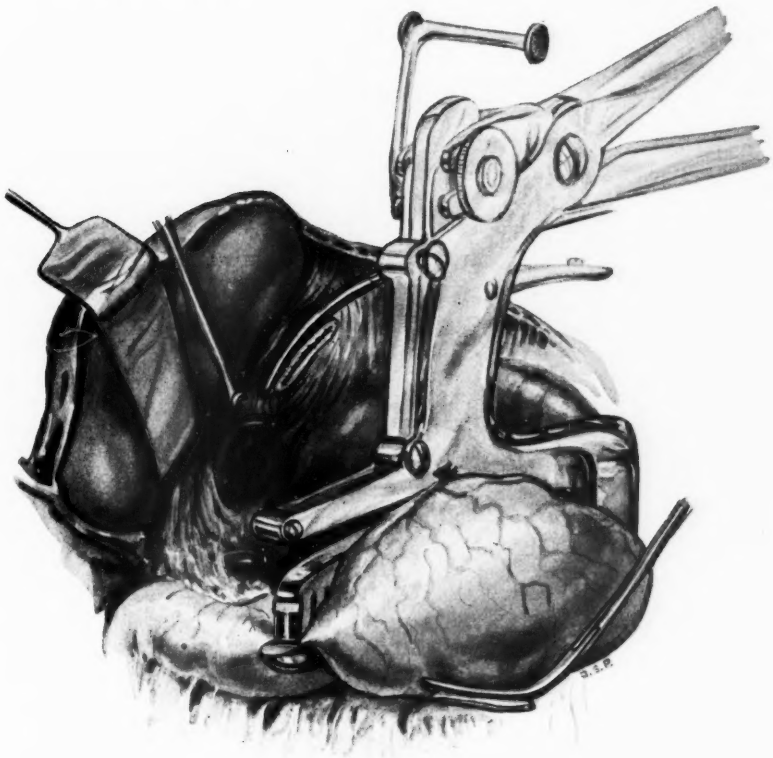


FIG. 2. The left gastric artery is transected distally from the esophageal branches. From the stump of the artery a biopsy specimen is taken. The fundus of the stomach is brought forward and clamped. The splenic artery and veins are also tied-off. The spleen is removed together with part of the tail of the pancreas during the resection.

every section of the stomach shall, wherever possible, be radically excised. However, the restoration of a passage from the esophagus through a remaining section of the stomach, or a "surgical" stomach, into the duodenum should in some way be accomplished if at all possible.

The position is, therefore, that in every case we are faced with the decision of how to combine a thorough, radical intervention with the necessity of providing for the optimum degree of postoperative function. When a compromise between these two facts cannot be found—and they often are diametrically opposed—we must either undertake a partial resection with the postoperative gastric function in mind or just accept the severe dysfunction resulting from too great a resection of the stomach, although in the latter case a complete excision of the pathologic tissue can never be guaranteed. If this question is viewed in a critical light, it becomes clear that the major part of the uncertainty arises from the fact that the special surgical procedures involving the fundus region contain a number of gaps. We know, of course, that with the carcinoma involving the cardia an abdominothoracic resection and intrathoracic esophagogastrostomy can give good follow-up results. But who cares for the responsibility of undertaking such an operation, with its attendant risks, for a lo-

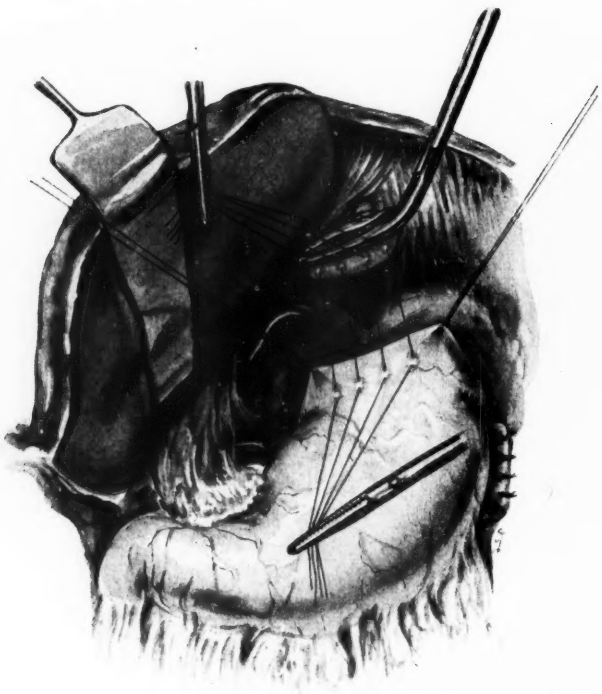


FIG. 3. The remaining prepyloric part of the stomach is closed. It is anastomosed at another site end-to-side with the intra-abdominal esophagus stump.

calized fundus carcinoma or even a subcardiac ulcer? On the other hand, the purely abdominal total resection for these conditions is an unnecessarily burdening operation: here, the prepyloric portion of the stomach, so important for the later digestive function, is sacrificed. The problem to be solved, therefore, is: the working out of a technique for the partial resection of the upper section of the stomach and the construction of an esophagoantrostomy by a purely abdominal intervention.

Attempts to fill this gap in gastric surgery have often been made. Nissen, for example, has shown that by leaving a small part of the fundus a reliable anastomosis between the intra-abdominal esophagus and the remainder of the stomach can be achieved. Nissen himself, however, because of the technical difficulties involved, gave up this technique in favor of another antrum-retaining resection. In this latter technique he anastomosed the esophagus subdiaphragmatically with a drawn-up loop of the jejunum. In this jejunal loop he implants the remaining antrum section with an end-to-side closure.

Although this solution may be considered for cases in which a small part of the antrum remains, it is not satisfactory for those occasions when larger prepyloric sections of the stomach may be preserved. Then a direct union with the intra-abdominal esophagus is required.

SUBDIAPHRAGMATIC FUNDUSECTOMY

Indications and technique. For the reasons given we have worked out the technique for subdiaphragmatic fundusectomy. This is a method of resection of the upper portion of the stomach by which a removal of part of

the fundus and a subdiaphragmatic union of the intra-abdominal stump of the esophagus with the remainder of the stomach can be carried out without much risk.

The indications for fundusectomy, in our opinion, are all isolated pathologic processes in the upper third of the stomach. The operation is indicated therefore, principally, for the radical treatment of the subcardiac, large, callous, hemorrhagic, and possibly malignant ulcers and for carcinomas of the fundus region which do not involve the cardia and the left gastric artery.

Pre-eminently suitable for fundusectomy are the localized carcinomas situated in the region of the greater curvature of the fundus because the lymph drainage of this region goes to the hilum of the spleen. The spleen as well as parts of the tail of the pancreas, in certain circumstances, may be removed without difficulty during fundusectomy. For the carcinomas situated on the lesser curvature of the fundus fundusectomy may be employed only in exceptional cases because the regional metastasis that occurs in the lymph drainage area of the celiac artery is generally more extensive, and thus requires an abdominothoracic resection.

For the success of subdiaphragmatic fundusectomy, two technical requirements must be absolutely observed.

1. Preservation of the esophageal branches of the left gastric artery which together with the ramifications of the inferior phrenic artery serve the intra-abdominal esophagus stump. This preservation is of the utmost importance for the success of the high subdiaphragmatic anastomosis which is performed.

2. The craniocaudal direction of resection by means of which at the beginning of the operation it is possible to judge with confidence the extent of the pathologic process. By means of biopsy specimens of the intra-abdominal esophagus stump and the left gastric artery, at the division by the esophageal branches, it is decided whether or not a partial resection of the upper part of the stomach by fundusectomy is advisable.

FIG. 4. The subdiaphragmatic fundusectomy is finished. The shape of the stomach is hardly changed by this "high Billroth I."

Special technique. In fundusectomy the abdomen is opened by means of an upper median laparotomy. The incision is extended to the left if necessary with notching of the cartilaginous rib arch (Marwedel's procedure). Then the cardia is dealt with. The esophageal branches are bluntly displaced medially and secured with suitable wound hooks or retractors (Fig. 1). The intra-abdominal esophagus is clamped superiorly with a soft jawed clamp and inferiorly with an ordinary clamp and immediately transected (Fig. 1). After ligaturing a few connections to the gastrolienal ligament the fundus may be pulled to the front. The left gastric artery, distal from the outlet of its esophageal branches, is now underrun and tied off. In carcinoma of the fundus a biopsy specimen and frozen section from the region of the artery stump as well as the intra-abdominal esophagus stump will tell us whether a fundusectomy is possible or not. If the trial biopsy shows neoplastic tissue, then an extended intervention must be car-

FIG. 5. Case 1. Encroaching process in the fundus region. X-ray picture suspiciously like a fundus carcinoma.

FIG. 6. The same case after subdiaphragmatic fundusectomy.

ried out with removal of the esophageal branches and the distal esophagus as far as to where the esophageal artery takes over the supply to the intrathoracic esophagus. If the biopsy is negative, then the fundusectomy may be carried out. The fundus is separated from the rest of the stomach and closed off by means of a Petz suture clamp (Fig. 2). The prepyloric stomach sac achieved in this way is anastomosed with the intra-abdominal stump of the esophagus (Fig. 3). It is of no importance which of the current techniques of anastomosis is chosen. The anastomosis will hold so long as the esophageal branches remain. If the esophageal branches of the gastric artery are damaged during the anastomosis then the success of the subdiaphragmatic anastomosis is very much endangered. Then, in spite of additional securing stitches to the diaphragm, the anastomosis may not be sound, and even a spontaneous perforation of the distal intrathoracic esophagus may occur as a result of a lack of tissue nutrition. In such cases it is better to avoid the subdiaphragmatic anastomosis and to carry out an intrathoracic anastomosis 3 fingerbreadths above the diaphragm. If the subdiaphragmatic fundusectomy succeeds, however, then in this manner a "high Billroth I" is achieved. This, with respect to the shape and function of the stomach, reproduces almost normal conditions.

Clinical reports. Two typical fundusectomy cases are detailed below.

CASE 1. A 60 year old male in very poor general health. Clinically, all signs of a typical cardiac orifice stenosis were present. Vomiting occurred after meals. Benzidine test on stool was always positive. X-ray examination showed a large encroaching process at the junction of the fundus and body lying near the greater curvature (Fig. 5). Operation showed a fist-sized tumor in the fundus region toward the posterior wall of the stomach, nearer the greater curvature. The tumor was localized and had not infiltrated during its growth. Macroscopically no metastasis was seen. A biopsy and frozen section showed the other areas to be free of neoplastic tissue. A typical subdiaphragmatic fundusectomy was carried out. The postoperative his-

FIG. 7. Case 2. Large callous, hemorrhagic, subcardiac ulcer, probably malignant.

FIG. 8. The same case after subdiaphragmatic fundusectomy.

tory was uneventful. A roentgenographic control (Fig. 6) showed a smooth esophageal passage. The contrast agent was carried over the stomach stump with good motility. The emptying of the pylorus was normal. Histologically, the diagnosis was adenocarcinoma of the stomach. The iron absorption test gave a normal serum iron level and a low uptake of iron, i.e., a sign of complete iron saturation of the body.

CASE 2. A 40 year old man, with a case history from 1944, clearly lowered general health, and several unsuccessful previous courses of medication management for peptic ulcer. Before admission to hospital, a 6 weeks' course of treatment, with the patient confined to bed, had proved unsuccessful. The presence of unbearable pain, vomiting, loss of appetite was noted; total serum protein was 6.0 grams per cent. The x-ray picture (Fig. 7) showed a deep, penetrating, subcardiac ulcer, hypersecretion, and suspected malignancy. At operation a tumor the size of a child's fist was seen. Macroscopically, no metastasis was apparent. A subdiaphragmatic fundusectomy was carried out. The postoperative course was uneventful. Because it had been discovered prior to operation that marked iron deficiency was present, iron was given by mouth and the patient placed on a high protein diet. Three weeks after operation the x-ray picture showed a typical postfundusectomy appearance with a smooth passage into the stomach. Seventy-four days after operation the patient was re-examined. The general condition was good: the weight had increased; hemoglobin 85 per cent; total serum protein 6.7 grams per cent; albumin 4.4 grams; globulin 2.3 grams. The serum iron level was normal. The x-ray picture (Fig. 8) showed a postfundusectomy appearance with normal conditions of motility. No pyloric spasm was present.

FOLLOW-UP STUDIES AFTER FUNDUSECTOMY

A few of the patients subjected to fundusectomy were thoroughly studied after the operation. The emphasis in these studies was laid upon the iron absorption ratio and proteolytic capacity of the fundusectomized stomach. Follow-up studies were first of all performed on 4 dogs that had been subjected to fundusectomy. The investigations were made 78, 142, 182, and 220 days after the operation. Three patients who had a fundusectomy were also investigated 74, 98, and 132 days, respectively, after the operation. The results of the absorption studies with respect to iron were found to be similar both in the experimental animals and in the pa-

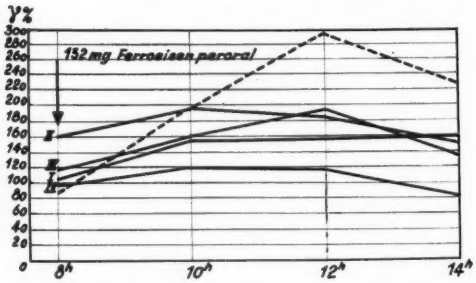


FIG. 9. Curves *I* to *IV* show the iron absorption of 4 fundusectomized dogs 78, 142, 182, and 220 days after operation. The curves show that a complete iron balance exists. The broken line shows, in comparison, the iron uptake of an animal with a two-thirds resection 191 days after the operation. This indicates a masked iron deficiency with increased absorption.

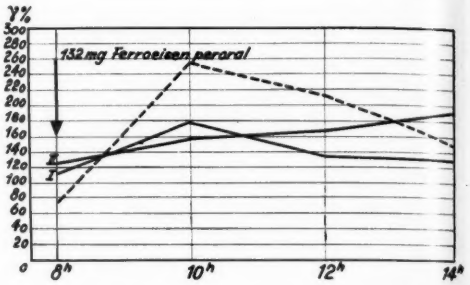


FIG. 10. Curves *I* and *II* show the iron absorption of 2 fundusectomized patients. The continuous curves show that a complete iron balance exists. The broken curve demonstrates, in comparison, the iron uptake of a patient who has undergone a two-thirds gastric resection. The increased uptake of iron denotes a masked iron deficiency.

tients. In all animals (Fig. 9) the fasting serum iron value lay within the normal range. The absorption curve following an oral loading dose of iron was quite flat. This is a sign of an existing iron balance. In comparison the broken curve shows the absorption ratio in an experimental animal (191 days after the operation) which had had a two-thirds resection of the stomach. This curve is typical of a masked iron deficiency with increased absorption. This masked iron deficiency (after a two-thirds resection) was demonstrable in a large number of observations on our patients who had had a two-thirds resection (G. Heinrich). In the first 2 patients with a fundusectomy (Fig. 10) the fasting value was within normal limits. The oral loading dose resulted in a flat curve thus indicating a complete iron balance. In comparison the absorption ratio in a patient with a two-thirds resection is shown by the broken curve. Here also the existence of a masked iron deficiency is clearly seen by the increased absorption. Especially interesting are the figures for iron absorption in the third case of fundusectomy (Case 2, Fig. 11). Curve *I* in this graph (broken curve) shows the ratio before a fundusectomy was performed because of a high ulcer. At this time there existed a low serum iron level and a poor absorption, resulting from a chronic ulcer hemorrhage with severe gastritis. Seventy-four days after the operation (curve *II*) the serum iron level had normalized. The oral loading dose thus shows an iron balance. This favorable state was obtained within a short time solely by the oral administration of iron which is indicative of the completely satisfactory absorption ability following fundusectomy. Here is to be seen an important advantage of the radical resection of a subcardiac ulcer by fundusectomy in comparison with the palliative resection of a high ulcer.

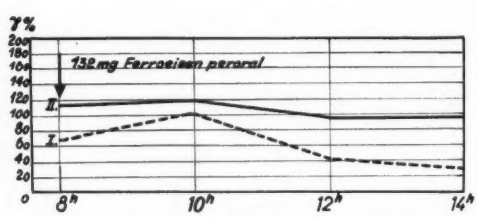


FIG. 11. Case 2. (v.s.) Curve *I*, broken curve, shows iron uptake before fundusectomy. Curve *II*, continuous curve, shows iron uptake 74 days after subdiaphragmatic fundusectomy. The serum iron level has normalized. The patient has an iron balance.

The investigations of the proteolytic capacity of the fundusectomized stomach by means of a skimmed milk test (Bramstedt) give favorable results, while in the two-thirds resected stomach following a Billroth II operation, a regurgitation of duodenal juice after 45 minutes is observed through

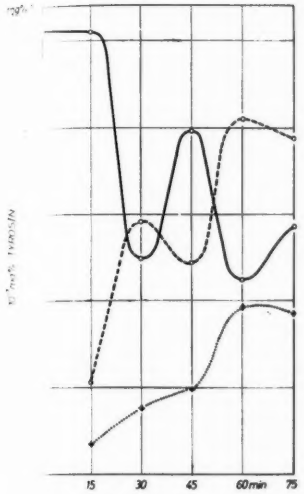


FIG. 12.

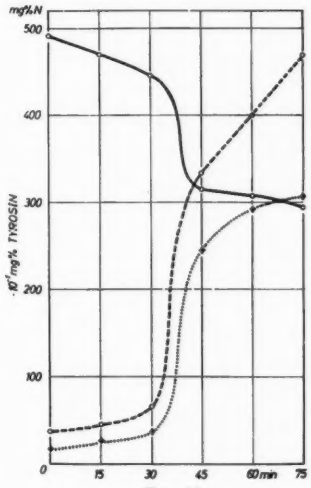


FIG. 13.

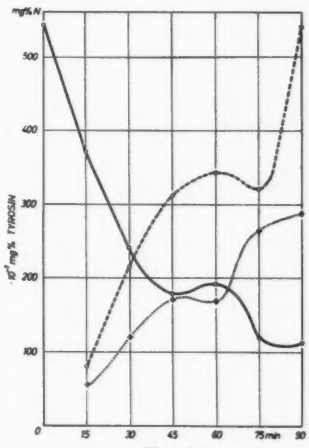


FIG. 14.

FIG. 12. Continuous curve shows total nitrogen; broken curve, nitrogen in trichloracetic acid filtrate; dotted curve, tyrosine equivalent after the Anson reaction. The regurgitation of duodenal juice is clearly seen on the total nitrogen curve.

FIG. 13. Proteolytic activity after subdiaphragmatic fundusectomy (on experimental animal). The proteolytic activity is practically normal. The stay in the remainder of the stomach is lengthened.

FIG. 14. Proteolytic activity after subdiaphragmatic fundusectomy (man). A delay in emptying of the stomach is not detectable. Proteolysis is within normal limits.

which nonsplit protein components are returned to the lumen of the stomach (Fig. 12). In the fundusectomized experimental animals (Fig. 13) there is no effect on the total nitrogen curve through the regurgitation of duodenal juice. The proteolytic capacity is hardly changed in comparison with normal. Because the milk remains somewhat longer in the remainder of the stomach (delayed fall of the total nitrogen curve) there is even a slight increase of the enzymatic activity. In the fundusectomized human stomach (Fig. 14) a clear cut delay in emptying has not been observed. The curve of the protein breakdown products shows that proteolysis is not significantly reduced in comparison with normal.

DISCUSSION

By means of the technique of subdiaphragmatic fundusectomy a gap has been closed in the practice of gastric surgery. By adhering to the resection technique given in this paper, esophagogastrostomy which has for long been feared in numerous surgical centers can be carried out from a purely abdominal approach without too great a risk. It is, therefore, possible to remove isolated pathologic processes in the fundus region of the stomach without removing the whole stomach as has previously been usual.

A considerable number of total resection or of two cavity interventions may be avoided by means of this high Billroth I. In certain respects, fundusectomy is even superior to the two-thirds resection of the stomach achieved by the Billroth II and its modification; for, after fundusectomy, neither the appearance of iron deficiency states, dumping syndromes, enterohepatic disturbances in protein metabolism, nor proteolytic insufficiency need be feared. Fundusectomy is that method of resection of the stomach which, together with the Billroth I for the distal section of the stomach produces the most favorable results in respect to noninterference with gastric function. Therefore, we definitely prefer fundusectomy to total re-

section and to the palliative Kelling-Madlener operation in high ulcers.

SUMMARY

1. Total gastrectomy is such a severely mutilating intervention that it should only be used in cases of dire necessity (*gastrectomie de nécessité*).

2. The choice of operative technique should be made in every individual case so that the optimal degree of radical resection is combined with the least possible loss of gastric function.

3. The development of an operative technique for partial resection of the upper section of the stomach is now one of the most important problems of gastric surgery.

4. The development of subdiaphragmatic fundusectomy has made a contribution in this respect.

5. The technique of subdiaphragmatic fundusectomy is described.

6. Two cases of typical fundusectomies are described.

7. Follow-up studies of iron absorption after fundusectomy have shown that, both in experimental animals and in human beings, dysfunction of iron absorption does not appear. This is in contrast to the two-thirds resection operation. Fundusectomy is superior to the two-thirds resection in respect of postoperative iron absorption function.

8. The proteolytic capacity of the fundusectomized stomach is not significantly limited. This is increased by the addition of the unaltered tryptic capacity of the duodenal juice so that an undisturbed total proteolytic action remains.

9. According to our experience, fundusectomy is suitable for the removal of local, limited neoplasms in the region of the fundus. It is, above all, recommended for the radical treatment of subcardiac, callous ulcers which are suspected of malignancy.

10. From June 1, 1954 to May 1, 1955—the period during which we have performed subdiaphragmatic fundusectomy—among 32 patients with pathologic processes in the cardiac and fundus region of the stomach, the number of patients suitable for fundusectomy was limited by critical selection to six. In these cases careful subdiaphragmatic fundusectomy was performed. They left the hospital in very good condition 2 to 4 weeks after operation.

REFERENCES

1. Allison, P. R. Discussion of Lahey and Marshall (8).
2. Brunschwig, A. Pancreato-total gastrectomy and splenectomy for advanced carcinoma of stomach. Cancer, N. Y., 1948, 1: 427–430.
3. Gütgemann, A. Totale Gastrektomie beim Magencarcinom. Chirurg, 1952, 23: 474–482.
4. Holle, F., and Heinrich, G. Die Bedeutung des präpylorischen Magenrestes u. seine Erhaltung durch eine subdiaphragmatische Fundektomie. Arch. klin. Chir., 1955, 280: 270–293.
5. Idem. Zur Indikation u. Technik der subdiaphragmatischen Fundektomie. Chirurg, 1955, 26: 164–169.
6. Idem. Arztl. Wschr., 1955, 327–330.
7. Lahey, F. H. Discussion of paper of Allen O. Whipple. Radical surgery in the treatment of cancer. Ann. Surg., 1950, 131: 812.
8. Lahey, F. H., and Marshall, S. F. Should total gastrectomy be employed in early carcinoma of the stomach? Experience with 139 total gastrectomies. Ann. Surg., 132: 540–564.
9. Madlener, M. Erfahrungen mit der "palliativen" Resektion beim cardianahen Magengeschwuer. Zbl. Chir., 1939, 66: 360–362.
10. Marshall, S. F. Carcinoma of stomach; plea for earlier diagnosis and more radical treatment. J. Internat. Coll. Surgeons, 1951, 16: 560–566.
11. Nissen, R. Erhaltung des Antrums statt totaler Gastrektomie bei der Operation des hochsitzenden Magenkarzinoms. Schweiz. med. Wschr., 1954, 84: 440–446.
12. ReMine, W. H., Dockerty, M. B., and Priestley, J. T. Some factors which influence prognosis in surgical treatment of gastric carcinoma. Ann. Surg., 1953, 138: 311–319.
13. Sweet, R. H. Total gastrectomy by the transthoracic approach; a subsequent report. Ann. Surg., 1953, 138: 297–310.
14. Tomoda, M. Agastrische pernizioese anaemie. Chirurg, 1954, 25: 49–58.
15. Wachsmuth, W. Kritisches zur Frage der totalen Gastrektomie. Deut. med. J., 1955, Vol. 6.
16. Winkelbauer, A. Die totale Gastrektomie in der Therapie des Magencarcinoms. Arch. klin. Chir., 1953, 271: 263.

THE MANAGEMENT OF CANCER OF THE MAXILLARY ANTRUM

DONALD RAINES, M.D., and ARTHUR G. JAMES, M.D., F.A.C.S., Columbus, Ohio

PRIMARY TUMORS of the maxillary antrum and nasal cavity are a relatively infrequently occurring entity. Sixteen primary carcinomas of the maxillary antrum have been seen at the Ohio State University Medical Center during the past 5 years. In most large series an average incidence of .35 per cent has been recorded. The purpose of this article is to present the therapeutic plan followed at the Ohio State University Medical Center including the technical details of the surgical and radiologic procedures employed.

The clinical material covered in this report was obtained from the 16 patients with primary carcinoma of the antrum who were seen from 1949 through 1953.

As Ohngren has stated, the earliest known excision of a tumor of the maxillary antrum was reported in 1671 by Richard Wiseman, a physician in the employ of Charles II of England. The earliest report of removal of the maxilla in toto was recorded by Walsham in 1879. Before 1900, Liston and Butlin noted metastases in retropharyngeal nodes and advocated lymph node dissection; they also proposed endotracheal anesthesia. Pickler, a German physician, reported 182 tumors of the maxilla surgically treated and he was probably the first to apply skin grafts to the raw surfaces of the postmaxillectomy cavity.

CLINICAL FEATURES

In the 16 cases seen, most of the possible variations of origin and extension of disease have been encountered. All of the lesions represented tumors primarily of the maxillary antrum. Fourteen of the 16 cases were of the superior portions of the maxilla and extended into the ethmoid area. Eight extended posteriorly into the pterygoid muscles in addition to the medial extension. In 2 patients the tumor had invaded the regions of the temporomandibular joint, and in 1 patient the tumor had ulcerated through the alveolar ridge. Orbital invasions necessitated exenteration of the orbit at the time of initial surgery in 8 patients, and 1 patient had orbital exenteration after destruction of the globe by later tumor invasion. Bony destruction was noted by roentgenographic examination in 15 patients prior to surgery and was confirmed at the time of surgery. In 5 patients extension was found into the base of the skull making total excision impossible. In 15 patients the lesions could be considered advanced, as there was evidence of bone destruction prior to surgery. One patient showed no roentgenographic evidence of bone destruction, but ulceration of the alveolar ridge was present clinically. This patient was a 63 year old white female who had had symptoms for 3 months. Dental extractions had been performed because of pain in the upper teeth on the right side. An ulcerated lesion developed subsequently in the site of the extraction, and a biopsy of this area disclosed carcinoma. A total maxillectomy was performed followed by implantation of radioactive cobalt for a total tumor dose of 7,000 roentgens.

The sex distribution in this series was 13 males and 3 females which does not concur with larger series in which the incidence has generally been 2 males to 1 female.

The age of the patients in this series ranged from 45 to 79 years. This figure, in general, agrees with most larger series.

Pathology. Of the 16 carcinomas seen, 13 were of the squamous cell type, 1 was a transitional cell carcinoma, 1 an epithelioma

From the Department of Surgery, University Hospital, Ohio State University Medical Center, Columbus, Ohio.

adenoides cysticum, and 1 an adenocarcinoma. In general this distribution corresponds to that found in other large series, especially a series of 127 cases primary in the antrum described by Watson of which he reported 89 per cent were squamous cell carcinoma.

There is no uniformity of opinion regarding the incidence of metastasis to regional lymph nodes. Our clinical studies disclosed metastatic lesions in 1 patient shortly after surgery. The difficulty in finding metastases lies basically in the clinical problem of observing the normal lymphatic drainage of the antrum, which is primarily in the retropharyngeal lymph nodes. The first palpable node involved is usually in the upper deep jugular chain. Therefore, when this is palpable, the disease is rather far advanced. The second most frequently involved node is in the submental area. It is of importance to note that despite the far advanced lesions found in 15 patients, there was clinical evidence of metastases in only 1 instance. This patient had an unrecognized pulmonary metastases which invaded the pleura and caused pleural effusion 1 month postoperatively. This patient was a 69 year old colored male with a history of nasal obstruction and facial swelling of only 3 months' duration. The lesion was found to be an adenocarcinoma which could not be totally removed. A total maxillectomy and orbital exenteration were performed to expose the tumor and remove the main mass. The residual tumor was subjected to a sponge mold containing radioactive cobalt for a tumor dose of 7,000 roentgens. An additional air dose of 2,400 roentgens was administered during the immediate postoperative course. The patient expired 1 month postoperatively as a result of pulmonary metastases.

Symptoms. The most common complaint encountered in this series was pain which was mentioned by 10 of the 16 patients as their chief complaint. Ten patients also complained of swelling of the cheek. Three patients presented with nasal obstruction, and 2, with alveolar ridge ulceration. It is obvious that the presenting complaints are related to the location of the tumor. Anteromedially located tumors cause nasal obstruction. Anterosuperior and lateral tumors cause swelling of the face, proptosis, and pain as the initial findings. Lateroinferiorly located tumors usually erode into the alveolar ridge. Posteroinferior and superior tumors may cause any of the symptoms mentioned depending on their extensions. In general, pain, swelling of the face, proptosis, alveolar or palatine ulceration, epistaxis, and nasal obstruction are the common symptoms seen.

Diagnosis. It is unfortunate that the diagnosis of these lesions is often made when the prognosis is poor, even though the chief complaint has been present for only a short period of time. The average duration of onset of complaint to time of first treatment of the tumor in this series was 8.6 months. Many cases were of much shorter duration than average. One patient with a complaint of pain in the left maxilla of 1 month's duration was found to have such an extensive tumor that radical maxillectomy and exenteration of the orbit were required. At the time of surgery, the lesion was found to invade the base of the skull and temporomandibular region. Complete surgical exenteration was not possible. It was quite evident that this tumor had existed for a long time prior to detection.

One 63 year old white male had noted weakness and pain over the left side of his face for 6 weeks. Roentgenograms showed bony destruction of the orbital floor, lateral maxillary wall, and base of the skull. On surgical exposure, the tumor was found to involve the maxilla, orbit, ethmoids, and the area of the pterygoid muscles. Implantation of the postoperative cavity with radioactive cobalt was necessary.

Another patient, a 79 year old white male, had complained of chronic sinusitis for many years. However, there was no change in his nasal complaints until 4 months prior to the diagnosis when he had noted pain in his cheek. Two months prior to surgery an empyema of the antrum was drained. This condition further obscured the diagnosis as

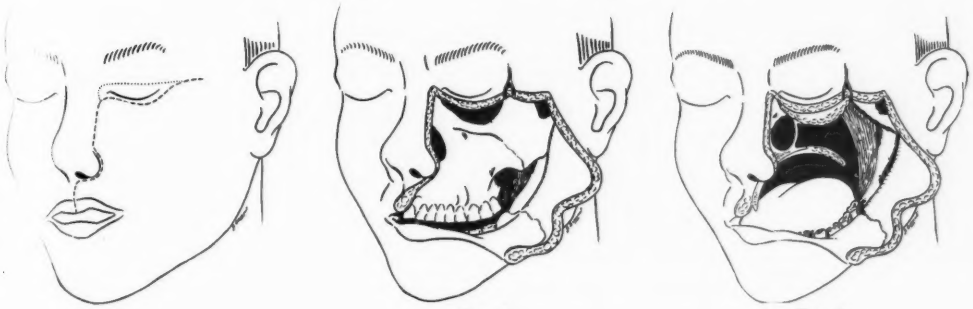


FIG. 1. FIG. 2. FIG. 3.

FIG. 1. Skin incision for approach to the maxillary antrum. Note finely dotted line for extension of incision if exenteration of the orbit is indicated.
FIG. 2. Reflection of skin flap showing exposure of the maxilla, nasal bone, and zygoma.
FIG. 3. Surgical defect remaining after resection of the maxilla.

it was believed that his symptoms were due to this infection. However, when the abscess continued to produce a purulent discharge, a biopsy revealed a well differentiated squamous cell carcinoma. Surgical removal was performed, and the tumor was found to involve the orbit, maxilla, ethmoid sinuses, sphenoid sinuses, and the main mass of the pterygoid muscles.

As can be seen by the foregoing, these patients were not aware of the disease which had existed for varying periods of time prior to the development of symptoms.

Following physical examination, roentgenograms of the sinuses are always obtained. If a tumor is suspected, aspiration or direct biopsy is performed. If these are not successful, two rather simple procedures may be used to explore the maxilla further. The choice depends on the location of the tumor. Anterior and medial tumors can be easily reached through an antral window made under the inferior turbinate. If further survey is necessary, the Caldwell-Luc or sublabial approach to the antrum is available.

The major difficulty in the establishment of an early diagnosis of maxillary tumors is the masking of the true pathologic condition by an inflammatory process. Mattick and Streuter point out that 88 per cent of their series showed clouding of the maxillary sinuses. In 81 per cent of the patients in this series the same findings were demonstrated, indicating the necessity for a more careful evaluation and follow-up study of patients with routine sinus disease.

TREATMENT

Surgical anatomy. The blood supply to the maxilla is principally from the internal maxillary artery and its terminal branches, and it is interrupted in removal of the maxilla. Prior ligation of the external carotid artery is not considered essential. Because of the wide anastomotic blood supply of the face and maxilla, the bleeding is not materially reduced by such ligation.

The facial nerve is interrupted peripherally. Function is lost because of removal of the facial muscles. The eye and mouth continue to function normally except in those cases in which the upper facial branches of the facial nerve must be sacrificed.

Surgical technique. The surgical treatment of tumors of the maxilla has become more radical in an effort to obtain a better survival rate. During the past 6 years, a total maxillectomy has been advocated in preference to the lesser procedures. By this procedure removal of the tumor in toto is more often accomplished as well as exposure of extensions of the tumor which might otherwise be overlooked. It is feasible to explore the ethmoid labyrinth and sphenoidal sinus

from the defect which persists after removal of the maxilla. The orbital periosteum may be examined, and extensions into the pterygomaxillary area may be exposed without difficulty.

The initial skin incision (Fig. 1) is outlined with a scalpel beginning inferiorly and splitting the lip in the midline up to the columella. An incision at right angles to the initial incision is made across the base of the nose into the nasolabial crease, and is extended around the ala and superiorly along the maxillary crest to the infraorbital ridge. The incision is curved laterally onto the lower eyelid. Special care is taken to make the incision as close to the tarsal border as possible in order to prevent the formation of postoperative lymphedema of the lower lid which occurs quite frequently when the incision is extended laterally across the face on the bony infraorbital margin. The skin incision is extended laterally over the zygomatic process. An incision of the mucous membrane is next made in the gingivolabial fold starting at the superior end of the initial lip-splitting incision. This incision is extended posteriorly to the posterior border of the maxilla. The skin flap is thus outlined. Superiorly, the skin flap is reflected from the tarsal plate and the infraorbital margin is exposed. The nasal cavity is entered along the margin of the maxillary crest. The outlined skin flap is elevated from the maxilla (Fig. 2). A margin of 1 centimeter of normal tissue is left over any tumor protruding beyond the bony wall. If there is no extension through the bone, the periosteum is exposed. Although this is an extensive incision, it is necessary so that the widest possible exposure of the antrum may be obtained.

The removal of the maxilla is now accomplished by separating the main attachments. First, the zygomatic arch is exposed, the lower attachment of the zygoma to the maxilla is freed, and the orbital periosteum is elevated. A perforation is made through the lateral wall of the orbit just beneath the attachment of the arch of the zygoma, and this attachment is transected with a Gigli saw. The nasal ethmoid orbital attachment is next severed with a chisel directed posteriorly to cut the maxilla from the ethmoid. Inferiorly, the palate must be split in the midline. An incision is made through the mucous membrane over the alveolar ridge extending posteriorly to the edge of the hard palate. This incision is then extended laterally along the posterior palatine margin to the initial mucous membrane incision. The posterior inferior attachment to the pterygoid plates is next severed with a hammer and chisel.

The hard palate is split in the midline. If teeth are present, the central incisor on the affected side must be extracted. The maxilla is then grasped with a large forceps and rocked from its position. The major bleeding now occurs due to severance of the internal maxillary artery. The initial hemorrhage is easily controlled by pressure, the artery is located, clamped, and ligated.

After removal of the maxilla (Fig. 3), the cavity is explored for extension of the tumor beyond the limits of previous examinations. Various possibilities of extension of the tumor exist. These are as follows:

Orbit.—The extension of tumor through the orbital periosteum usually necessitates the exenteration of the orbit. The orbital contents are removed by blunt and sharp dissection, and the optic stalk is clamped and ligated as it contains the opthalmic artery.

Ethmoidal, sphenoidal, and frontal sinuses.—The initial skin incision is extended superiorly around the inner canthus of the eye to the supraorbital margin. The nasal bones are exposed and removed with rongeurs. The nasofrontal duct is exposed and the ethmoid labyrinth is exenterated including the medial orbital wall. The sphenoid and frontal sinuses may be opened without difficulty. The most vital structure to be avoided is the cribriform plate.

Skin.—Invasion of the superficial skin may necessitate the removal of all or a portion of the cheek. The cavity thus created is packed with gauze and allowed to heal.

FIG. 4.

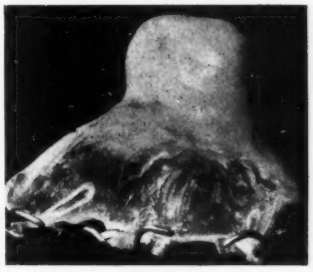


FIG. 5.

FIG. 6.

FIG. 4. Palatal opening after resection of the maxillary antrum which permits adequate visualization for postoperative recheck examinations.

FIG. 5. Plastic dental mold which is used for intracavitary radiation.

FIG. 6. Roentgenogram of a mold loaded with radioactive gold seeds which has been placed in the palatal defect shown in Figure 4.

later, plastic reconstruction or a prosthesis can be used to fill the defect.

Pterygoid muscle and temporomandibular joint area.—Further extension of the tumor into the muscle or temporomandibular joint may necessitate removal of the pterygoid muscles and the ascending ramus of the mandible. No special difficulty is encountered with this procedure.

The cavity thus created usually has a normal mucous membrane over the nasal septum. However, the interior of the skin flap and the muscle bed of the maxilla are denuded. A split thickness skin graft is obtained and sutured in place covering all denuded areas. The initial skin incision is approximated with interrupted sutures of No. 0000 silk. Special care is taken to approximate the vermillion border carefully.

A vasoline gauze pack is allowed to remain in the cavity for from 3 to 6 days. After its removal, the cavity is cleaned daily with a mixture of hydrogen peroxide and water in equal parts. Crusts are meticulously removed. Care is taken not to damage the skin graft. Feedings are administered through a nasogastric tube. An attempt is made to give a high protein, high caloric diet. In approximately 10 days after operation, the cavity is fitted with a sponge prosthesis. The feeding tube is removed and oral feedings are started. With the sponge mold in place, soft diet is taken without difficulty. This sponge is removed by the patient and cleaned after each meal. The patient is also taught to irrigate the cavity daily.

After the cavity is thoroughly healed, a dental prosthesis may be made to fill the palatal defect.

Radiation therapy. Some alteration has been made in the plan of radiation during the past 5 years at the Ohio State University Medical Center because of the advent of radioactive cobalt, gold, and iridium. Because of the accessibility of the defect (Fig. 4), intracavitary radiation has been considered the most advantageous type to use. Twelve of the patients received postoperative irradiation in this manner. Two others received external high voltage radiation, and 2 received none. The irradiated cases are divided into two groups. The first group consists of those in which the tumor has extended beyond the limits of surgical removal. In these patients, as much tumor as possible has been removed. This surgery is followed by radioactive implantation. The second group consists of those in which, although the tumor was completely removed, the lines of excision were not considered sufficiently wide.

The actual method of implantation has been altered some during the past years. Initially, a sponge prosthesis was used. In the depth of the sponge, pellets of radioactive material were placed. The source of radiation was designed to deliver adequate radia-

tion at the periphery of the defect. The dosage varied from 6,500 to 8,000 roentgens. Later it was believed that a method of better localization of the radiation therapy over the areas of tumor or suspected tumor would be of advantage. Therefore, a mold of the cavity was made with dental plaster (Fig. 5). After it was hardened, radioactive seeds (Fig. 6) were implanted in those areas of the mold which were to come in contact with the areas on the walls of the surgical defect containing or suspected of containing residual tumor. This mold was easily applied through the defect in the palate. There was no difficulty in maintaining its position in any of the patients. A tumor dose of 7,000 roentgens was generally administered. The technique employed in the use of these radioactive substances at the Ohio State University Hospital is described elsewhere in the literature (1, 2, 3).

DISCUSSION

As has been noted from the cases presented, early diagnosis of cancer of the antrum is seldom made. In most of the cases evidence of bony destruction was present by the time the patients were hospitalized. If these tumors could be discovered while they were still in the confines of the bony antrum, it would be comparatively easy to obtain a high percentage of curative results simply by resecting the maxilla. In the past, surgery and irradiation have been used individually and in combination in the management of these tumors. External high voltage radiation therapy was found to have marked limitations because: first, it is difficult to deliver a uniform, adequate tumor dose to the entire lesion; second, it is practically impossible to sterilize tumor cells once they have invaded bone; third, much sepsis results from radiation therapy without previous surgery because of the lack of drainage of debris and damaged tissue. Surgery alone is inadequate in many of the cases since extension of tumor to areas not resectable is common. The use of the routine postoperative radiation with high voltage external therapy has the limitation of not delivering a uniform dosage, and consequently areas of overirradiation and underirradiation result.

We believe that the method which we have advocated overcomes most of these objections. The involved tissue is first removed without regard for cosmetic appearance. Involved adjacent structures are removed when feasible. Great care is taken at the time of resection to note the location of residual or possible residual tumor. The plastic molds are then made and selectively loaded with radioactive substances to treat these areas.

The surgical defect is not a serious problem. Dental prosthetics can be made to fill this gap so that speech and deglutition are not impaired. During the immediate postoperative period (usually 6 months), a sponge obturator forms a very adequate temporary prosthesis. The defect due to orbital exenteration is usually covered with a gauze patch which may later be replaced with an appliance containing a false globe that attaches to an eye glass frame.

SUMMARY

1. Data concerning 16 patients seen at the Ohio State University Medical Center with primary carcinoma of the maxillary antrum are presented.

2. The therapeutic plan including surgical and radioactive techniques is discussed.

3. The advocated treatment is: adequate surgical resection, and a plastic mold containing radioactive substances to the defect to provide the necessary irradiation.

REFERENCES

1. James, A. G., Henschke, U. K., and Myers, W. G. The clinical use of radioactive gold (Au^{198}) seeds. Cancer, 1953, 6: 1034.
2. James, A. G., Williams, R. D., and Morton, J. L. Radioactive cobalt as an adjunct to cancer surgery. Surgery, 1951, 30: 95.
3. Idem. The use of radioactive cobalt in non-resectable head and neck cancer. Cancer, 1951, 4: 1333.
4. Mattick, W. L., and Streuter, M. A. Carcinoma of the maxillary antrum. Surgery, 1954, 35: 236.
5. Ohngren, L. G. Malignant tumors of the maxillo-ethmoidal region. Acta otolar. Stockh., 1933, Suppl. xix, 1: 1.
6. Watson, W. L. Cancer of para-nasal sinuses. Laryngoscope, 1942, 52:22.

A SKIN BANK FOR POSTMORTEM HOMOGRAFTS

JAMES BARRETT BROWN, M.D., F.A.C.S., MINOT P. FRYER, M.D., F.A.C.S., and THOMAS J. ZAYDON, M.D., St. Louis, Missouri

THE NEED FOR RESURFACING large areas of the body, without delay, frequently arises when adequate skin grafts from the patient himself are not available because of debility or the wide extent of the burn. In many such situations, the best recourse is to homografts taken from postmortem sources. A method for collecting and using these grafts is the first essential in the establishment of a skin bank. The next element is the preservation of postmortem homografts for later use so that supplies of these "biologic dressings" may be in reserve when fresh grafts are not available, as in serious disasters when there are multiple needs for these grafts to save lives.

Having a stockpile of banked skin on hand to meet emergencies is important because even large medical centers may have long periods without a satisfactory postmortem skin donor.

Homografts of human skin from postmortem sources were first used on this service in 1927, in consideration of possible survival of fetal skin as homografts, and a brief history of postmortem uses in general was included in our report in 1953 (5).

Extensive studies have been made on the preservation and banking of skin. So far, there is no final decision as to the optimum conditions for the preservation of viable skin, although freeze-dry preservation is established as it is for other tissues.

In patients with large skin losses, biologic dressings with homografts often prove lifesaving, and, in the event of civilian disaster or a national emergency, large amounts of banked skin could play a vital part in saving many lives. Formerly 30 or more live donors have been used for 1 badly burned patient, with the attendant operative time and expense, anesthetics, time loss, postoperative wound care, and patient discomfort; or a single donor was stripped of a huge amount with necessary hospital care and debilitation. At present, large amounts of skin may be taken from a single donor after death and used immediately or set aside in the skin bank for later use.

Closing the wounds with homografts diminishes the loss of fluids, proteins, and electrolytes; there is respite from pain and frequent dressings; infection is diminished; there is diminished fibroblastic response in the wound; a mechanical barrier to trauma is established; there is a stimulus for the patient's own epithelization so that good progress of healing may occur by the time the homograft is absorbed. There is always a remarkable improvement in the general condition of the patient proportionate to the amount of open wound coverage, so that he is prepared for the application of successful permanent autografts from his own body.

Extensive partial thickness burns (which may cause death) also can be dressed with homografts, thus providing a biologic dressing until there is spontaneous healing.

Homografts may be applied repeatedly in successive "crops" after preceding grafts have been absorbed until autografts can be removed from the patient himself, in graded amounts if it should be necessary. According to the condition of the patient and the availability of autografts, there may be advantage in alternating strips of autografts with viable homografts or covering one part as on the face or hands with autografts and

From the Plastic Surgery Service, Department of Surgery, Washington University School of Medicine, and Barnes Hospital, St. Louis.

This work has been aided by a Hartford Foundation grant to Barnes Hospital.

other areas with the homografts. The maximum benefit for the patient from any homografts that are used is the goal.

There is no hindrance to the autografting of the granulating wound after absorption of a homograft or after its intentional removal. The optimum time for autografting is always considered on an individual basis, however, the procedure being carried out as soon as the patient can tolerate it.

It is generally accepted at this time that in humans all homografts will "take," and will survive 2 to 12 weeks, but eventually will be lost except in identical twins (3). Much investigation is being done to try to find out if one living human can accommodate to foreign viable tissue and retain it in symbiosis, or change it to his own peculiar gene structure or enzyme systems. So far this has not been accomplished, except that it may be possible in patients with agammaglobulinemia where there may be enough tolerance to foreign viable tissue because of a lack of intrinsic cellular antibody response, to allow a homograft to survive, as has been reported by Good and Varco in a 7 year old boy. Microscopic study of homografts reported from this service in 1942 (6) supports this finding. Many other suggestions have been made, including the use of ACTH, antihistamines, and sublethal x-ray dosage, but so far an identical twin graft is the only one that can be counted on for permanence. There is some trouble in the discussion because of not distinguishing between a "take" with survival for a few weeks, and permanent survival that continues to function as normal skin, as in an autograft or in one from an identical twin. In the event that homografting could be made permanent, banking of viable skin would take on immense added importance. It would have to be viable skin to start with and then preserved, with or without nutrients at +4 degrees C. and perhaps from −10 to −70 degrees C.; but freeze-dry preparations are nonviable.

At this time viable skin naturally seems to be the most desirable material for homografting, but it is recognized that nonviable skin, frozen or freeze-dry, or possibly prepared otherwise and stored, may form a protective dressing almost as long as fresh viable grafts, and these may prove to be the main reliance in emergency. Several other methods of preservation are being investigated here at this time. It is even possible that preserved zoografts from animals or fowls could be used as effectively, but the collection of human skin will probably be easier and more acceptable than the use of zoografts.

It would be still more acceptable, of course, to find a synthetic or natural covering that would last as long as the homografts and thus eliminate the need of and the attendant trouble of procurement and storage, and this problem also is being investigated.

Autotissue cultures may come to fulfill some of the basic needs and, if so, it is barely possible that homografts will not be needed. But so far there has been no tissue culture production of the full complement of the skin which is necessary for normal living. Sheets of epithelial cells will not suffice for normal skin with its pad of derma, so that along with the rapid growth in tissue culture of auto-epithelium would have to go some mechanism for the production of skin instead of just epithelial cells. The epithelial cells, however, would hasten healing and general improvement, but would not avoid scarring and contraction and distortion, nor reproduce a feature.

Having sufficient sources of human skin is one of the most important points of the whole process, and it is hoped that sufficient impression on the public may be forthcoming to allow the taking of postmortem thin layers of skin, which in no way disfigure the body. As has been stated (4, 5), it is a chance for human worth and dignity to be carried a little farther toward the grave, in that a patient who dies may save the life of another who would die without this help.

All physicians, especially those on house staffs, can be alerted to the need for an

adequate stock of available skin. Upon the death of any patient, if free of malignant disease or of any transmissible disease or dyscrasia, an attempt can be made to obtain permission for removal of skin grafts. In some states (Missouri) permission can be given by the patient before death for postmortem examination, and a clause may be included for the removal of skin. In other states the nearest survivor "owns" the body and permission must be obtained from him, and it seems more discreet and proper to abide by the wishes of the next of kin. If a proper approach is made and the need explained, it is usually possible to obtain consent. Permission for removal of skin grafts should always be in writing and duly witnessed. Also, permission may be obtained for removal of skin even if a postmortem examination is denied. If necessary, the relatives may be shown the need for skin by attending a dressing of a severely burned child or may be shown a photograph of the patient in urgent need of skin coverage. It can be explained that there will be no apparent deformity to the skin of the donor and also that only areas covered by clothing, as the trunk and thighs, are used. An expression of thanks by words or letter from the family of the recipient, the patient himself, or the attending physician is always given. The awarding of a small certificate from the service involved may be considered.

SIMPLE REFRIGERATOR BANKING

The simplest method of banking viable skin homografts is to fold them in saline antibiotic gauze sponges and store at refrigerator temperature (3° to 5° C.)

It is best to remove the skin as soon after death as possible. In the event of any delay, the body should be kept refrigerated. Viable grafts thus can be obtained after 24 hours' delay, and even up to several days, as final death of skin does not occur at the same time as the cessation of circulation in general or somatic death.

The postmortem skin grafts are best removed in the operating room, with the sterility and dignity of any operative procedure. The donor sites are cleaned with soap and shaved. The skin is prepared with ether and alcohol and sterile drapes. Long sheets of thin split skin grafts are removed from the thighs and trunk, using the free-hand knife and suction retractors or the electrodermatome, one-third to one-half the thickness of the skin, according to the donor area and general thickness of the skin. The glue dermatome is not necessary and is cumbersome. The take will be most sure with thin grafts, and as these grafts are not permanent, thickness is not necessary. The grafts may be used immediately or are folded on themselves, dermal surface to dermal surface, wrapped in antibiotic saline moistened fine mesh gauze and stored in a sterile jar at refrigerator temperature until needed.

Skin that is banked at this temperature has a rather marked cellular metabolism; however, these preserved skin grafts will be viable and take well up to 21 days. Some take may be obtained even over a month, becoming progressively poorer after 3 weeks' storage. Pepper, using autograft studies, reported that rabbit skin survived not longer than 5 weeks at 0 degrees C., 21 days at 13 degrees C., 11 days at 22 degrees C., 7 days at 30 degrees C., 3 to 5 days at 37 degrees C.

This method of banking is probably the simplest; a minimum of materials is necessary; little time is required in preparation; ordinary refrigeration is readily available; the skin can be used immediately after removal from the refrigerator; generally no anesthesia is necessary as the grafts are quickly snubbed in position with the dressing; and the skin is viable for 3 weeks with a lesser percentage of take being obtained even after longer periods of banking. With saline gauze alone, no provision is made for nutrient materials or buffering the acids produced by the living tissues.

The percentage of takes with refrigerated skin homografts is about as good as with autografts. The homografts will survive for

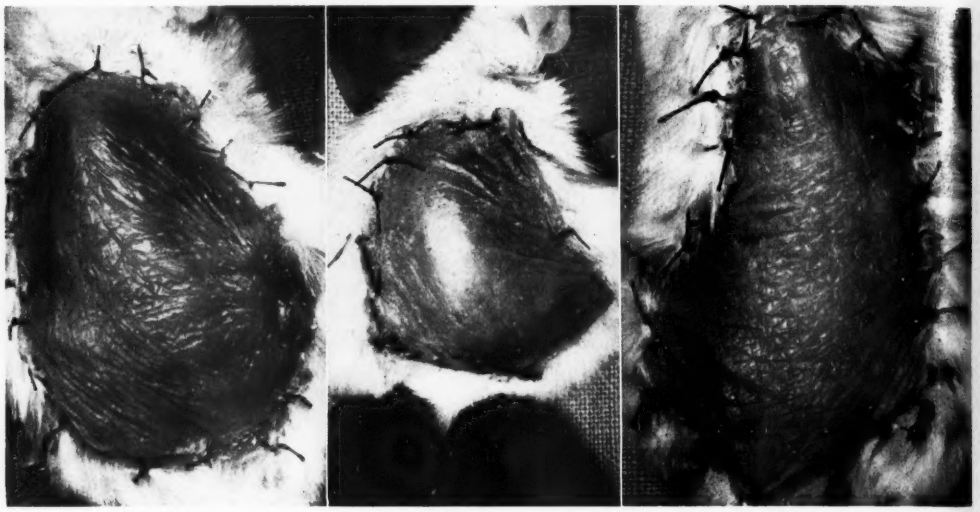


FIG. 1. FIG. 2. FIG. 3.

FIG. 1. Human skin banked 8 weeks at +4 degrees C. with only saline gauze, grafted on mouse and shown after 5 days. There is loosening of epidermis but dermis retained 10 to 12 days.

FIG. 2. Human skin graft preserved in nutrient at +4 degrees C. for 10 months shown on mouse 1 week after application. Epidermis partially loosened, viable dermis retained 13 to 16 days.

FIG. 3. Human skin preserved in glycerol-nutrient solution at −40 degrees C. for 1 year grafted on mouse and shown after 7 days. There is epidermal loosening, but dermis retained 12 to 15 days.

several weeks, and on occasion for months. The grafts generally absorb or "melt away" in a clean fashion without infection, just fading away gradually and leaving a clean, granulating base.

It may be possible to obtain 2 to 3 thicknesses of graft from the same area on the back of the donor if needed. Thickness of the grafts may be an advantage in length of survival if they once take, as the derma of the graft seems to persist the longest.

We are investigating the advantages of turning to lyophilization or low temperature storage methods in the event that skin simply stored as described is not used within a few weeks. This double method of preservation may give the grafts a further lease on usefulness.

NUTRIENT MEDIA

To prolong the storage time at ordinary refrigerator temperatures, (3° to 5° C.) mixtures of various body fluids, salt solutions, and antibiotics have been used. Ten per cent serum or 10 per cent plasma in a buffered salt solution, with added penicillin and streptomycin (50 units per c.c.), are usually depended on. Plasma is more readily available than serum and has the added buffering potential of fibrin. Blood is not satisfactory as a media since the blood cells contribute to acidification and exhaustion of the medium; therefore, a noncellular fluid as serum or plasma is preferred. Phenol red may be used as an indicator so that as the acid products of cellular metabolism accumulate in the nutrient media, color change occurs. Hyatt (12, 13), using plasma in Earle's solution, has reported good results after 6 months of storage at about 3 degrees C., the take and persistence comparable to freshly removed homografts. The nutrient solution is generally changed about every 8 weeks.

Skin to be preserved in this manner may be wrapped in gauze which is moistened with the nutrient media, or the grafts may

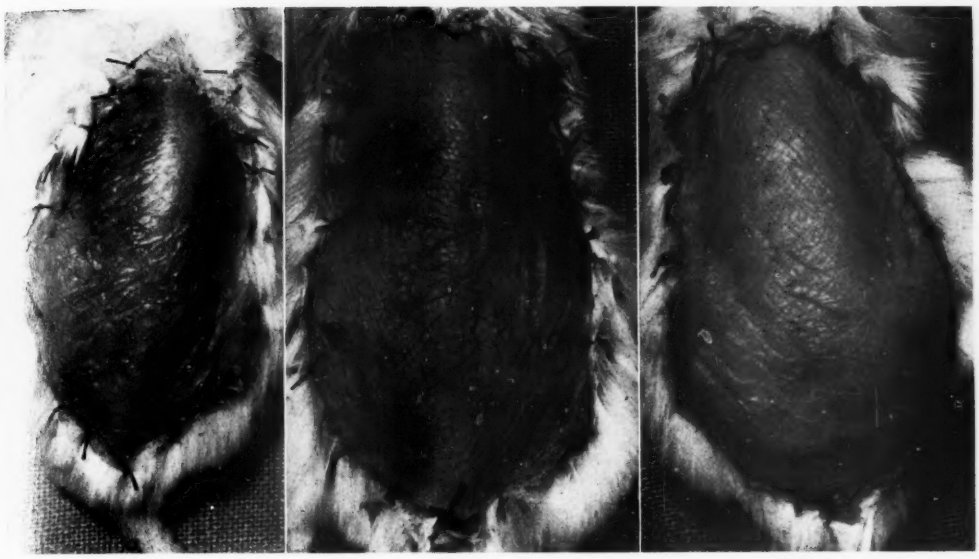


FIG. 4. FIG. 5. FIG. 6.

FIG. 4. Human skin graft banked at −80 degrees C., glycerol-protected, using air jacket for slow freezing and sealed to eliminate CO_2 atmosphere, shown on mouse after 5 days. Some epidermal loosening, dermis retained 12 to 14 days.

FIG. 5. Lyophilized human skin on mouse 4 days after application. Epidermis intact for 5 to 6 days, dermal covering retained for 14 to 16 days.

FIG. 6. Human skin removed from refrigerated body 7 days after death, shown here 10 days after grafting on mouse. Epidermis intact 12 to 14 days. Dermis soft, pliable, fixed to bed 17 to 20 days.

be just covered with the media. Allgower and Blocker have found optimum viability to occur when the media volume is approximately 1 cubic centimeter for each square centimeter of skin. The grafts should be stored in the presence of air to support metabolism since exclusion of oxygen has been found to be detrimental, according to Hanks and Wallace in studies using 10 per cent serum and rabbit skin stored at 6 to 8 degrees C. The question of getting the nutrient to large sections of skin and the excessive amount of nutrient required pose problems in large scale storage.

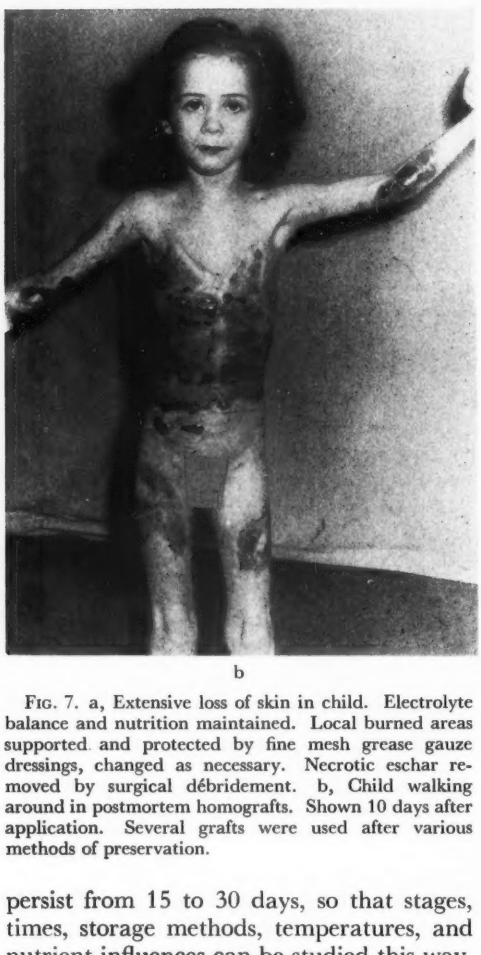
It possibly is not necessary to change the storage fluid as long as it remains clear and sterile, and frequent changing has been shown to be harmful in tissue culture studies, although this has not been verified clinically.

Storage in the presence of these solutions makes available to the graft a nutrient and serves to dilute and buffer the acids resulting from cellular metabolism. The method is relatively simple, the solutions are easily prepared, the storage time is prolonged over that with saline, ordinary refrigeration is adequate, and the grafts may be used immediately after removal from storage.

Adenosine, which has been suggested to prolong the storage time of blood, may prove of some value in skin preservation. These investigations are now being carried out. With adenosine there has been better than 70 per cent viability of blood cells preserved at 4 degrees C. for periods of 5 to 12 weeks, compared to control studies of 3 or 4 week survival.

In the study of viability of grafts, the grafting of human skin on the experimental mouse (reversed zoograft) with good clinical observation has been of value. Human skin grafts will take on denuded areas of the mouse and

a



b

FIG. 7. a, Extensive loss of skin in child. Electrolyte balance and nutrition maintained. Local burned areas supported and protected by fine mesh grease gauze dressings, changed as necessary. Necrotic eschar removed by surgical débridement. b, Child walking around in postmortem homografts. Shown 10 days after application. Several grafts were used after various methods of preservation.

persist from 15 to 30 days, so that stages, times, storage methods, temperatures, and nutrient influences can be studied this way.

Since, however, homografts that have been preserved by what may be considered nonviable methods may persist on a wound almost as long as a viable homograft, for the most accurate determinations of viability of grafts under different methods of preservation or for any final decision of persistence it would be necessary to use autografts from the animals themselves or possibly depend on inbred animals that will retain permanently homografts from one another. This method, of course, could be used on human workers or on identical human twins, but the laboratory animals would save a great deal of time and discomfort and procedure. Grafts from such inbred animals have been called "isografts" by workers at the National Institute of Health.

Pomerat (23, 24) believes that the best test of viability is tissue culture. He states that in vivo there is always the possibility of marginal or deep tissue confusing the issue.

Goodpasture, Douglas, and Anderson reported on the growth of human skin on the chorioallantois membrane of developing chick embryos. Tenery and McDowell have carried out experimental studies on 88 grafts by similar transplants and have reported on the gross and microscopic evidence of viability. They conclude this method to be a practical indication of the viability of an experimental human skin graft, the viable skin appearing intact, smooth or moderately wrinkled, and yellowish-pink; on section the architecture was intact with the cells staining normally.

Studies of permanence of grafts, on the other hand, have to be made in inbred animals that approximate identical twins, or in laborious transfer of autografts or in identical twin grafts in willing human workers.

LOW TEMPERATURE BANKING

There have been few reports on the clinical use of cold preserved skin, and there have been many differences of observation as to viability and take after low temperature storage, with some reports that skin has failed even to survive on storage below 0 degrees C.

Low temperature banking of skin and other tissues has been carried out with the

preservation of viability for prolonged periods.

The protective use of glycerol. We are studying the banking of skin after pretreatment with 15 per cent glycerol in Earle's and in Ringer's solutions, along with various combinations of nutrient media and other solutions (and also without glycerol). These have been stored at −10, −20, −40, and at −79 degrees C.

Thin split skin grafts are placed in one of the glycerol solutions for 60 to 90 minutes. The grafts are blotted with gauze and are placed in a glass jar. This jar is put in a second container, providing an air jacket for the slow lowering of the graft temperature in a dry ice-alcohol mixture (−79° C.). To conserve space, only the inner jar is used in storage. When these grafts are needed, they are rapidly thawed by immersing the jar in a 37 degrees C. water bath, or by immediately plunging the grafts in sterile Ringer's solution kept at 37 degrees C. until fully thawed. After this rapid thawing, to remove the glycerol, the grafts are kept in Ringer's or Earle's solution for 1 hour, at room temperature, prior to transfer.

It seems possible that skin could be carried to −79 degrees C., banked for prolonged periods of time, and then thawed without damaging the major portion of the cells. Slow (air chamber) cooling seems to give better preservation of viability than rapid cooling, and rapid thawing gives better viability than slow thawing. Even though physiologic and chemical changes with some deterioration do take place at −79 degrees C. and even at −180 degrees C., the cellular and biochemical processes are slowed down and viability may be preserved for prolonged periods of time. After the skin is thawed from the low temperature state, it tends to deteriorate more rapidly than fresh skin and should be used promptly.

Glycerol has no cytotoxic action and it has been shown that even isolated epidermal cells can survive exposure to 90 per cent glycerol for 8 hours at 0 degrees C. and to 80 per cent glycerol for 2 hours at room temperature. By the inclusion of glycerol in the preserving media the skin can be protected against lethal effects of low temperature and of thawing. The exact mechanism of the antifreeze (and what might be called "antithaw") protection of glycerol is not certain. While glycerol may not prevent the formation of ice crystals, it is known that it changes the structure of the low temperature solid; that it dehydrates to some extent; that it lowers the freezing point of water; that its viscosity promotes a high degree of supercooling. It is believed that to be effective, the glycerol must diffuse into the graft and probably into its cells. So that, in this method, it seems safe to pretreat with glycerol long enough to afford adequate protection at the low temperatures. Various cells may differ in their permeability to glycerol,

a

b c

FIG. 8. a, Extensive full thickness skin loss in child. b, Postmortem homografts giving adequate coverage 10 days after application. With life thus saved, permanent coverage with sheets of child's own skin then done in stages. c, Healed with own skin. Secondary contractures avoided.

and a large mass of cells, as in a skin graft, will take a longer time for glycerol diffusion than small isolated groups of cells. It has been stated that perhaps a good criterion of successful glycerol preservation is the successful preservation of viability at low temperatures, which is the end point desired clinically.

Skin is probably more sensitive and vulnerable to its thawing from low temperature than conversion to it. The possibility of using diathermy for very rapid thawing of tissues has been explored and in some instances has not been found to thaw tissues fast enough. A radar type of apparatus, operating at a very high frequency and with high power, which should provide sufficient energy, has been suggested by Lovelock for rapid thawing.

Rabbit skin has been used experimentally by Medawar (2, 20) and found to survive up to 500 days or longer at −79 degrees C. after impregnation with glycerol prior to temperature reduction of the banked grafts. On autografting of skin so preserved, these grafts did not show any distinguishable changes from unstored skin grafts in fine structure, color, epithelial growth rate, and differentiation of glands and hairs. Controls which had been pretreated with Ringer's solution or saline alone are inferior, with sparser hair and depigmentation, and, in general, are poorer cosmetically. This is believed to be a very satisfactory method for long term storage of viable skin.

LOW TEMPERATURE STORAGE WITHOUT GLYCEROL PROTECTION

This method is being investigated, and Skoog has done experimental work with skin stored at low temperature. Viability was assessed by oxygen consumption, using the Brancroft-Warburg method. Thawed skin which had been stored at −70 degrees C. for varying periods up to 28 weeks showed a relatively constant oxygen consumption. Human split skin applied as homografts, after storage at −70 degrees C. up to 13 months, was as successful in take as fresh homografts in 3 clinical trial areas.

Other studies have been carried out by Strumia and Hodge on the preservation of human skin prior to autografting, using just enough citrated bank plasma to cover the grafts, carried to −20 to −25 degrees C., stored at this temperature and thawed with a 37 degree C. water bath. These grafts were used up to 61 days with only a slight inferiority to fresh autografts. The results were not markedly affected by the time of storage; in fact, in several instances the frozen grafts took better than the control fresh grafts.

VITRIFICATION

Ultrarapid cooling leads to vitrification and is theoretically to be preferred since it is believed that the formation of ice crystals is prevented, eliminating the mechanical damage to the cells by these crystals. Luyet (16–19) has carried out extensive studies showing viability of various cells and tissues after ultrarapid freezing and thawing.

Ultrarapid cooling of skin has been carried out after precooling to just above the freezing point. This temperature lowering has been carried out by plunging the grafts into liquid nitrogen (−196° C.). Even better results were obtained if the grafts were partially dehydrated by immersing them in ethylene glycol for 20 seconds to 3 minutes. As the speed of cooling required to vitrify varies with the water content, this preliminary dehydration facilitates vitrification. After ultrarapid cooling the skin was stored at −70 degrees C. Keeley, Gomez, and Brown report a high percentage of survival after 44 and 66 days but not after 123 days. Buchanan found no difference from fresh controls in dog skin which was quick frozen to −190 degrees C., kept up to 1 hour, and autografted.

It seems that with mammalian skin, using the criteria of continued growth and cell division, better viability is maintained by banking after slowly lowering the temperature of the grafts than by ultrarapid methods. Pryde and Jones believe that it is difficult to achieve vitrification of water and

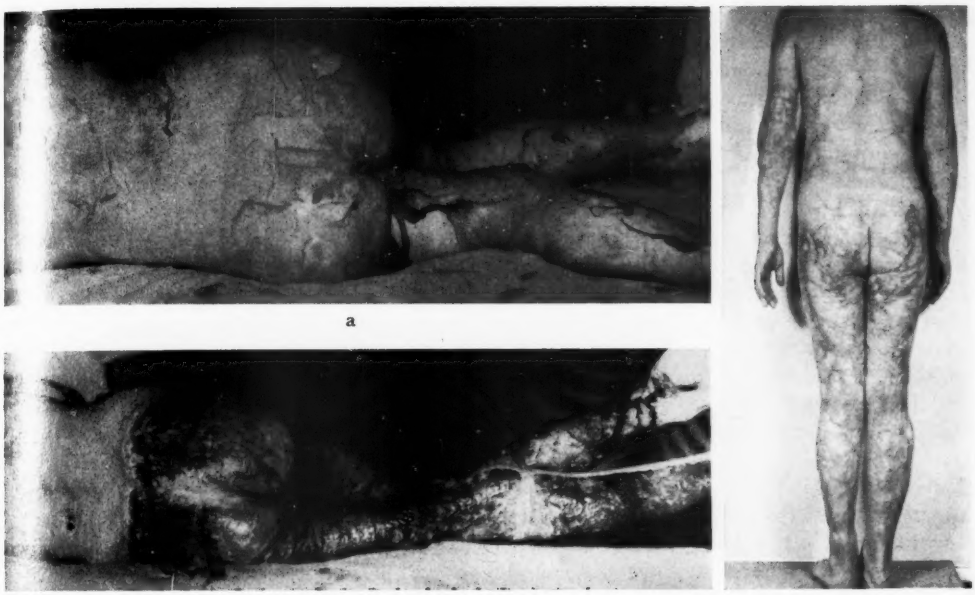


FIG. 9. Life saved by the use of homografts in extensive deep burn. a, On admission before débridement. Received whole blood; fluids and electrolyte balance and nutrition maintained. Healing of superficially burned areas encouraged by fine mesh, grease gauze; pressure dressings applied immediately and subsequently as necessary. b, Widespread full thickness loss surgically débrided of necrotic eschar permitted coverage with life-saving homografts in 3 weeks' time. c, Solid permanent healing completed with autografts.

that it will remain in the vitreous state only at temperatures below −130 degrees C., reverting to crystalline ice above this temperature.

LYOPHILIZATION (FREEZE DRYING)

Lyophilization is a process in which the skin is frozen, and then under high vacuum the ice is sublimed, that is, the ice evaporates without melting, to a low temperature condenser. Freeze-dry methods of skin preservation may give a practical long term storage of nonviable skin, as with blood vessels.

Webster, using lyophilized skin as an autograft, reported an 80 per cent take, after 17 days' preservation, and stated, "There is no question of fact that this skin graft, which was frozen at −72 degrees C. and dried by the lyophilizing process, actually survived this treatment and persisted as living skin, although it was a less satisfactory transplant than the control fresh graft that was immediately transplanted."

The possibility of some cells escaping death by such processes is being investigated; to be certain autografts are used or inbred animals in which homografts will survive.

Rabbit skin will not remain viable in drying from the frozen state to below a final water content of 25 per cent, and no mammalian tissues have been found to withstand drying to below 10 per cent residual moisture content. With lyophilized skin, which has been dehydrated to the total water content of less than 1 per cent, tissue culture has not been able to demonstrate living cells. Gross appearance of skin is misleading as to the degree of drying, and the final water content should be determined to substantiate the degree of lyophilization.

Hyatt and associates (12, 13) believe freeze-dried skin to be an excellent means

of long term skin preservation, serving the function of temporary wound coverage as well as fresh homografts. These can be simply shelf stored at room temperature, are easily transported, stable for prolonged periods of time, and easily prepared for use by the addition of saline for 30 minutes prior to use. Hyatt used lyophilized skin on a young patient which lasted approximately 2 weeks, but states that the skin did seem to disappear earlier than homografts from multiple donors which had been preserved in balanced salt solution.

After freeze-dry skin is moistened, it looks and feels like a fresh split skin graft. Pate has applied lyophilized skin to 20 patients and states that no surgeon could tell which is the freeze-dried skin and which is the fresh homograft, and that it sticks and looks like a viable graft.

Buchanan and Lehman have desiccated skin grafts in the frozen state and transplanted them in the dog after plasma hydration. These persisted in the grossly normal state for periods up to 22 days. They state that the tissue persistence is not influenced by the time of preservation, whether used as autografts or homografts. A single clinical trial suggests that it may prove of value as a temporary covering. The skin persisted for 12 days, after which the patient died of complications.

The technique of lyophilization has been published many times and frequent changes in details are made; but the technique is mentioned here in summary for completeness. It is essentially that reported by Creech, DeBakey, and Cooley.

The skin grafts are taken under sterile conditions, but when necessary they may be passed through several basins containing antibiotic saline solution. The grafts are spread out over a firm, coarse, wrinkled gauze material to obtain maximum surface exposure and free air circulation during drying. If needed, after the skin has been placed in the containers, liquid ethylene oxide is added to destroy microorganisms and it is poured off after 20 minutes. The containers are then immersed in a dry ice-acetone mixture and connected to the lyophilizer. When freeze-drying is complete, the tubes are vacuum sealed and shelf stored at room temperature.

In early trials, many hours were needed to lyophilize skin effectively. With recent modifications of technique and use of an efficient freeze-drying apparatus having outlets for 25 tubes, drying is complete (less than 1 per cent water content) in less than 3 hours' time. When there is need for the skin, reconstitution is effected by soaking the tissue for 30 minutes in a 37 degree C. saline solution containing 500,000 units of penicillin and 1 gram of streptomycin to the liter.

Viable homografts may last longer and may give a more secure biologic closure of wounds and provide a more normal surface covering than nonviable, such as freeze-dry, homografts. Viable homografts may even spread out slightly.

Lyophilized skin, however, has a place in the temporary coverage of raw surfaces, even if it serves only as a purely mechanical function. This preparation of skin may prove to be the most practical in national emergencies, but so far it has not been tried on such a scale. In such emergencies if grafts with other methods of preparation persist longer, these of course will be the most useful.

Viability may not be the most important factor; the major consideration may be just the structural preservation of the skin membrane which will adhere to the wound. If this should prove to be true, then other methods of preservation of skin itself or some other substitution may be found that will seal a wound shut as long as the homografts. In other words, the final answer may not be at hand but at least these present methods may be used to save lives until better methods are available.

TISSUE CULTURE

Tissue culture or the storage and growth of skin in a nourishing and oxygenated

medium has been carried out for a long period. Culture grown epithelium might be produced and grafted and might be of value as a temporary coverage. If fast methods of propagation of autograft cultures can be accomplished and if these cultures can be regrafted onto the injured patient, a valuable method will be forthcoming, whether the full complement of the skin is obtainable or not. The result would be similar to scar epithelium, and effort could be directed toward growing the fully normal skin in culture.

SUMMARY

Of vital importance is the necessity of acquainting the public with the great need for postmortem grafts for seriously injured patients. Any individual, even before death, might experience satisfaction in knowing that after his death he may be of service in saving the life of another. At present, large amounts of life-saving tissues are being allowed to go to waste. Civilian needs for skin might be supplied and administered by a central agency in the same manner as blood banks. Mobile teams of trained personnel could be organized to remove large amounts of postmortem skin to be banked for use wherever and whenever necessary. National defense could include studies and direction of a national plan for this procedure.

Viable homografts taken after death and used immediately or preserved by satisfactory banking methods have all the advantages of homografts taken from live donors, plus the added advantage of ease of procurement and absence of disability in live donors. The skin homografts are biologic dressings for burns and open wounds. They are of tremendous importance in providing a viable body covering and respite from pain and fluid loss. Less extensive care is needed and a marked general improvement of the patient results.

Preservation and storage of skin for use in emergencies or in disasters is a goal of a skin banking system. If the grafts could be kept viable, they might serve the most useful purpose, but nonviable methods of storage are practical and may prove valuable for long term stock supplies. A method has been observed clinically of evaluating viability of skin homografts after application to an experimental animal or to the human recipient. Tissue culture is said to be satisfactory for this purpose, but it is not in common usage and may fail to show tissue growth of banked skin which may yet be viable on transplant. Observation of growth on chick embryos is another method. Determination of metabolism and respiration by the Warburg technique is of experimental value but may be too technical for ready applicability.

It is thought that supplies of banked skin should be developed and be available, in view of the pall of war and inevitable mass injuries ever over us. It would be highly difficult to secure the tremendous number of necessary donors for skin homografts at the exact time they are needed. Further, the removal of the skin grafts at the time of disaster would add to the existing confusion and work load of surgical services at that time. However, a fresh supply still might be of great advantage and could be accomplished when adequate team work was at hand.

There are still many problems to be worked out: general acceptance by the public and by physicians themselves, applicability of nonviable skin, storage problems for viable skin, and the most valuable plastic surgery problem of all—permanent skin homograft survival. All of these would be of inestimable value in the saving of numerous lives now being lost for want of satisfactory wound coverage.

The use of homografts from postmortem sources can save the lives of many severely burned patients. A simple direct method for doing this is outlined here which can be used in any hospital now without special equipment.

If the fresh postmortem grafts can be used without having to go through storage processes, they give the best coverage and protection to the patient, even though their re-

moval from the body (refrigerated) has been delayed several hours or even days. Thus, a skin bank is actually in existence, even if the postmortem donor patient supplies the storage for the skin until it is used.

The unsolved problems of storage of grafts need not hinder the use of fresh postmortem homografts (or live donor ones) to save lives. It is evident now that the method described for the use of fresh or banked postmortem skin provides necessary amounts of coverage material as biologic dressings so that the mortality in severe burns is reduced.

REFERENCES

1. Allgower, M., and Blocker, T. G. Viability of skin in relation to various methods of storage. Texas Rep. Biol. M., 1952, 10: 1-21.
2. Billingham, R. E., and Medawar, P. B. The freezing, drying and storage of mammalian skin. J. Exp. Biol., Lond., 1952, 29: Sept.
3. Brown, J. B. Homografting of skin: with report of success in identical twins. Surgery, 1937, 1: 558-563.
4. Brown, J. B., and Fryer, M. P. Postmortem homografts to reduce mortality in extensive burns. J. Am. M. Ass., 1954, 156: 1163-1166.
5. Brown, J. B., Fryer, M. P., Randall, P., and Lu, M. Postmortem homografts as "biological dressings" for extensive burns and denuded areas. Ann. Surg., 1953, 138: 618-629.
6. Brown, J. B., and McDowell, F. Epithelial healing and the transplantation of skin. Ann. Surg., 1942, 115: 1166-1180.
7. Buchanan, F. T., and Lehman, E. P. An experimental study of preservation of skin grafts by the freeze-drying process. Surgical Forum 1951; American College of Surgeons. Pp. 637–642. Philadelphia: W. B. Saunders Co., 1952.
8. Creech, O., DeBakey, M. E., and Cooley, D. A. Preparation and use of freeze-dried arterial homografts. Ann. Surg., 1954, 140: 35–43.
9. Good, R. A., and Varco, R. L. Successful homograft of skin in a child with agammaglobulinemia. J. Am. M. Ass., 1955, 157: 713–715.
10. Goodpasture, E. W., Douglas, B., and Anderson, K. Human skin grafted upon the chorioallantois of chick embryos. J. Exp. M., 1938, 68: 891.
11. Hanks, J. H., and Wallace, R. E. Relation of oxygen and temperature in the preservation of tissues by refrigeration. Proc. Soc. Exp. Biol., N.Y., 1949, 71: 196.
12. Hyatt, G. W., Turner, T. C., and Bassett, C. A. L. New methods of preserving skin, bone, and blood vessels. Naval M. News Lit., 1951, 18.
13. Hyatt, D. W., Turner, T. C., Bassett, C. A. L., Pate, J. W., and Sawyer, P. N. New methods for preserving bone, skin and blood vessels. Postgrad. M., 1952, 12: 239–254.
14. Keeley, R. L., Gomez, A. C., and Brown, J. W. Experimental studies on methods of skin preservation. Plastic & Reconstr. Surg., 1952, 9: 330–344.
15. Lovelock, J. E. Biophysical aspects of the freezing and thawing of living cells. Proc. R. Soc. M., Lond., 1954, 47: 1.
16. Luyet, B. J. Freezing and drying. Ed. by R. J. C. Harris, 1951.
17. Idem. Colloid Chemistry. Ed. by J. Alexander, 5, 859.
18. Luyet, B. J., and Gehenio, P. M. Life and Death at Low Temperature. Brodynamica, Normandy, 1940.
19. Luyet, B. J., and Hodapp, E. V. Revival of frog's spermatozoa vitrified in liquid air. Proc. Soc. Exp. Biol., N.Y., 1938, 39: 433–434.
20. Medawar, P. B. The storage of living skin. Proc. R. Soc. M., Lond., 1954, 47: 62–64.
21. Pate, J. W. Preservation and Transplantation of Normal Tissues. P. 173. Boston: Little, Brown & Co., 1954.
22. Pepper, F. J. Studies on the viability of mammalian skin autografts after storage at different temperatures. Plastic & Reconstr. Surg., 1954, 6: 250.
23. Pomerat, C. M., and Lewis, R. B. Methods for analysing thermal stress with tissue culture techniques, preservation and transplantation normal tissue. P. 141. Boston: Little, Brown & Co., 1950.
24. Idem. Thermal stress and tissue culture. Texas Rep. Biol. M., 1953, 11: 307.
25. Pryde, J. A., and Jones, G. O. Properties of vitreous waters. Nature, Lond., 1953, 170: 685–688.
26. Skoog, T. An experimental and clinical investigation of the effect of low temperature on the viability of excised skin. Plastic & Reconstr. Surg., 1954, 14: 403–417.
27. Strumia, M. M., and Hodge, C. C. Frozen human skin grafts. Ann. Surg., 1945, 121: 860.
28. Tenery, J. H., and McDowell, F. A method for determining the viability of experimental human skin grafts. Surgical Forum, 1952; American College of Surgeons. Pp. 623–626. Philadelphia: W. B. Saunders Co., 1953.
29. Webster, J. P. Refrigerated skin grafts. Ann. Surg., 1944, 120: 431.

AN ANALYSIS OF PULMONARY RESECTION IN 513 CASES OF TUBERCULOSIS

F. [illegible] COLE, M.D., F.A.C.S., and F. H. ALLEY, M.D., F.A.C.S., Memphis, Tennessee

IN THE PRESENT ARTICLE a statistical analysis is presented of 513 pulmonary resections for tuberculosis, performed at the West Tennessee Tuberculosis Hospital in Memphis. These are all the resections performed from the opening of the hospital in December 1[illegible] through August 1953. The postoperative observations range from 1 year to 5½ years in length. Most of the operations were done by members of the surgical resident staff, with the active supervision of senior staff members. A total of 26 surgeons are listed as operators in the surgical records of the 513 patients. A continuity of choice of therapy, operative methods, and postoperative management has been achieved by the conference method of patient selection and by a review of each patient, his progress, and the operative specimen within 2 weeks following the surgical procedure. Long term postoperative therapy is planned at that conference, influenced by the condition of the patient, findings at the operation, and the gross and microscopic characteristics of the lesions in the resected specimen.

For purposes of study, pertinent information about these 513 patients was coded, tabulated, entered on punch cards, and separated by mechanical means. A tremendous welter of figures and tables comes out, from which a few have been selected to show materials, results, and factors influencing the outcome of the patients.

The patients ranged in age from 9 to 64 years. There are 337 white, and 176 negroes in the group, which contains 3.5 per cent minimal, 34.5 per cent moderately advanced, and 61 per cent far advanced tuberculosis. Bilateral involvement was present in 60 per cent, and a positive sputum was found in 95.3 per cent. There was a wide diversity in the clinical condition of the patients at the time of surgery, and pulmonary involvement varied from asymptomatic "coin lesions" to the totally involved lung of advancing destructive tuberculosis. Preoperative treatment has included bed rest in all cases. 83.6 per cent had some adjunctive therapeutic procedure on the homolateral side, while 28.3 per cent had contralateral measures.

The period of this study includes years of great change in the therapy of tuberculosis, with a rapid decline in the frequency of collapse therapy, an increase in excision, and a tremendous improvement in antimicrobial drugs and in the techniques of their use. The change in the extent of pulmonary resection is shown in Table I. In our hands, pneumonectomy has decreased from 36 per cent in 1949 (Table I) to 5 per cent in the last 100 operations. Lobectomy and lobe plus segmental resection have remained fairly constant, but segmental excision has increased from 2.1 per cent in 1950 to 41 per cent in 1954. These changes reflect more efficacious drug therapy, and also the fact that the early years included many retreatment cases, and failures from other therapeutic measures. Bronchostenosis dictated many of the early pneumonectomies, while it is uncommon today.

Table II is a compilation of the mortality rate in the 513 patients. The upper part of the table shows the deaths that occurred within 90 days. There is definitely greater hazard involved in right sided operations than in those on the left, and in detailed studies, the increased death rate is in pneu-

From the West Tennessee Tuberculosis Hospital and Department of Surgery, University of Tennessee College of Medicine, Memphis, Tennessee.

TABLE I.—EXTENT OF RESECTION

	1949 Per cent	*1950 Per cent*	*1951 Per cent*	*1952 Per cent*	*1953 Per cent*	*1954 Per cent*
Pneumonectomy	36	26	21.5	24.2	8.8	5
Lobe or lobes	52.8	62.5	65.7	49.2	50	44
Lobe plus segmental	9	9.4	7.8	10.5	9.8	10
Segmental	2.2	2.1	5.0	16.1	31.4	41
No. of cases	89	96	102	124	102	100

TABLE II.—MORTALITY RATE IN 513 PATIENTS

	No. of patients	*No. of deaths*	*Per cent mortality*
Early deaths (90 days)			
White			
Right side	190	7	3.7
Left side	147	4	2.7
Colored			
Right side	84	3	3.6
Left side	92	1	1.07
Totals	513	15	2.9
Late deaths, tuberculosis or surgery		10	1.9
Other deaths		8	
*Total mortality		33	6.4

*White 6.2 per cent; colored 6.8 per cent.

TABLE III.—PRESENT STATUS RELATED TO AGE

	Group 1	*Group 2*	*Group 3*	
Age, years	*Per cent*	*Per cent*	*Per cent*	*No. of cases*
0–19	94.0	3	3	68
20–49	83.6	8.9	7.5	390
50–69	86.3	6.4	7.3	55
Totals	85.4	7.8	6.8	513

monectomy and in right upper lobe resections. There is a slightly lower early mortality in negroes than in whites. All of the early deaths in negroes followed pneumonectomy. The early mortality totals 2.9 per cent. Ten patients have succumbed to complications of surgery or to tuberculosis later than 90 days following surgery, but 7 of these deaths were directly related to surgical complications. Only 3 patients who had uneventful recovery and discharge from the hospital have later developed progressive tuberculosis and died. The total surgical and tuberculosis mortality to date is 25 (4.9 per cent). Coronary occlusion, ruptured peptic ulcer, trauma, and cerebral vascular accident have accounted for 8 additional fatalities. The cumulative mortality is 6.4 per cent. There is little difference between the races.

Regarding the present condition of the 513 patients, from 14 months to 5½ years following operation, reliable current information was obtained in all but 17—a 96.7 per cent follow-up. Of the total group, 85.4 per cent are classified as good results (group 1). These include (75 per cent) patients with essentially no disability, leading normal useful lives, 48 patients (9.4 per cent) are asymptomatic but must live sheltered lives, either because of functional limitation, or the possibility of reactivation of residual disease. Another 5 patients (1 per cent) have some surgical complication present. None of the people have positive sputum. The group classified as questionable (group 2) includes 18 patients under treatment for tuberculosis (3.5 per cent) but without positive sputum. Most of these will probably eventually recover completely. Five patients (1 per cent) have positive sputum persistently, and most of these will probably die of their disease. The 17 patients (3.3 per cent) who could not be found are also listed in the questionable group. These 40 patients who may yet shift into either of the other groups total 7.8 per cent of the series and are called questionable. The poor group (group 3) includes 2 pulmonary cripples, 25 fatalities from tuberculosis or from surgery, and 8 fatalities from other causes—a total of 35 patients—6.8 per cent.

The remainder of this presentation is a study of the factors that influence these results.

Table III is a study of the results by ages. The total figure is divided into the 3 groups mentioned before. There are 68 patients operated on under 20 years of age. They do better than average. In those 55 patients over 50 also the tuberculosis is under better control than in the average, although the mortality is a little higher. The patients under 20 have less chronic disease, while those over 50 are probably selected with a little more care.

Table IV relates the present condition to race and sex. White females and colored males do better than their opposite sexes. The mortality is highest in white men—10 per cent. Again there is no significant difference between the races.

Table V relates the present condition to length of illness. Long standing disease obviously is less satisfactory in its response to treatment than is more recent illness, and 4 years seems to be about the dividing line. Long standing disease results in a larger increase in mortality than does advanced chronologic age.

In Table VI the extent of resection is tabulated against present condition. The less extensive resections result in more satisfactory outcome. The pneumonectomy mortality (12.7 per cent) is higher than one would expect. Unfortunately, the majority of patients requiring pneumonectomy were seen early in our experience, when drug therapy was less efficient and surgical technique not as well perfected.

Table VII shows the influence of drug therapy. Patients who received no drugs or miscellaneous courses of drugs were treated early in the series, and at that time drug therapy was given in the less favorable cases. There is little difference in the results obtained. The long term combined chemotherapy has a very definite relationship to improved results, decreased mortality, and lessened complications.

Table VIII relates present status to date of operation. There is a progressive improvement in results over the years. This is not due to the gradual attrition of passing months on the group operated upon early, as is demonstrated by the lower figures. The eventual results are closely related to the condition at 90 days postoperative. In 1949, a surgical complication remained in 10 per cent of patients at 90 days postoperative, and 6.7 per cent were dead. In 1953, 1 per cent were complicated and none dead. These 96 patients are all still alive.

Table IX shows the present status of patients related to the occurrence of surgical complications. Surgical complications have a greater deleterious effect on the outcome than any other single factor. The uncomplicated cases are 89.2 per cent good and have a total mortality of only 2.3 per cent. Those having complications are 78 per cent good and 14.5 per cent dead. In a detailed study of the cases, there is no predictable liability to complication—good risks, poor risks, young and old, white and colored—all may do well, or may have trouble. The incidence of complications has decreased from 37 per cent in 1949 to 24 per cent in 1953. The principal decrease has been in spread of pulmonary disease which has come from a high of 8 per cent in 1950 to less than 1 per cent in the past 2 years. Miscellaneous surgical complications, not specifically related to tuberculosis, have also decreased from 12 to 2 per cent. These mishaps, including shock, hemorrhage, embolic phenomena, and phlebitis, become less frequent with increasing experience of the staff. Bronchopleural fistula has remained rather constant, although empyema as a sec-

TABLE IV.—PRESENT STATUS RELATED TO RACE AND SEX

	Group 1	*Group 2*	*Group 3*	
	Per cent	*Per cent*	*Per cent*	*No. of cases*
White	85.5	7.7	6.8	337
Males	81.8	8.9	10.1	149
Females	88.3	7.4	4.3	188
Colored	85.3	8.0	6.7	176
Males	88.7	4.2	7.1	71
Females	82.9	10.5	6.6	105
Total				513

TABLE V.—PRESENT STATUS RELATED TO LENGTH OF ILLNESS

	Group 1	*Group 2*	*Group 3*	
Period of time	*Per cent*	*Per cent*	*Per cent*	*No. of cases*
Less than 12 mos.	89.9	6.7	3.4	149
12–48 mos.	87.1	7.4	5.5	217
More than 48 mos.	78.2	9.5	12.3	147
Totals	85.4	7.8	6.8	513

TABLE VI.—PRESENT STATUS RELATED TO EXTENT OF RESECTION

	Group 1	*Group 2*	*Group 3*	
Type of resection	*Per cent*	*Per cent*	*Per cent*	*No. of cases*
Pneumonectomy	79.7	7.6	12.7	118
Lobe or lobes	86.7	8.4	4.9	286
Lobe and segment	83.4	8.3	8.3	48
Segment	91.8	4.9	3.3	61
Totals	85.4	7.8	6.8	513

TABLE VII.—DRUG THERAPY PRIOR TO SURGERY

	Group 1		*Group 2*		*Group 3*		*Totals*	
	No.	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*
No drugs	135	81.3	16	9.6	15	9.1	166	32.3
Miscellaneous	88	81.5	11	10.2	9	8.3	108	21
Long term combined	215	90	13	5.4	11	4.6	239	46.7

TABLE VIII.—PRESENT STATUS RELATED TO DATE OF OPERATION

Year	*Group 1 Per cent*	*Group 2 Per cent*	*Group 3 Per cent*	*No. of cases*	*90 days postoperative — Complication present*	*Dead*
1949	69.7	16.9	13.4	89	10.1	6.7
1950	80.2	8.3	11.5	96	7.3	2.1
1951	86.2	6.9	6.9	102	2.9	3.9
1952	92.7	3.2	4.1	124	.8	2.4
1953	94.1	5.9	0	96	1.0	0

TABLE IX.—PRESENT STATUS IS RELATED TO SURGICAL COMPLICATIONS

	Group 1	*Group 2*	*Group 3*	*Totals*
No complications				
No.	303	30	8	341
Per cent	89.2	8.5	2.3	66
Mortality, per cent				2.3
Complications				
No.	134	11	27	172
Per cent	77.9	6.4	15.7	34
Mortality, per cent				14.5

TABLE X.—FATE OF PATIENTS WITH COMPLICATIONS

	Group 1 Per cent	*Group 2 Per cent*	*Group 3 Per cent*	*No. of cases*	*Per cent occurrence*
Bronchopleural fistula	72.2	4.4	23.4	47	9.1
Spread	73.2	7.6	19.2	26	5.7
Delayed expansion	91.7	5.6	2.7	36	7
Chest wall infection	90.1	6.6	3.3	30	5.8
Miscellaneous	64	9	27	33	6.4

ondary complication is now rare. No effort is made to subdivide bronchopleural fistula into late leaks, and large bronchus breakdown. Anything requiring prolonged drainage, or redrainage is considered to be a fistula. Expansion difficulties include residual fluid, excessive pleural reaction, spaces undrained by original tubes that slowly absorb, and atelectasis. Chest wall infections, while still occurring, are much less severe and few secondary operations are necessary.

In Table X the fate of patients having surgical complications is detailed. The percentage occurrence of the complications is also noted.

Bronchopleural fistula and pulmonary spread are highly dangerous. Delayed expansion and chest wall infection increase morbidity, but the end result is satisfactory in a high percentage of both. "Miscellaneous" is a highly fatal condition, including as it does hemorrhage, shock, and embolism.

SUMMARY

In summary, this paper presents a survey of the first 513 resections for tuberculosis from the West Tennessee Tuberculosis Hospital. The period of postoperative observation ranges from 14 months to 5½ years. Reliable current information is available in 96.7 per cent of the patients. A satisfactory result has been obtained in 85 per cent, with 8 per cent somewhat doubtful, and 7 per cent definitely poor. The total death rate from tuberculosis or surgery is 5 per cent of the patients.

There is a dividing line in the middle of 1952, following which time mortality, complications, and results have been decidedly better than before. This improvement coincides with the arrival at operation of patients who had completed long term chemotherapy. Since then, the resection of residual disease has represented the majority of the surgery, and we find ourselves removing less and less tissue from more and more patients. Another influential factor in the results is the avoidance of operative complications. Expeditious surgery, careful dissections, meticulous hemostasis, accurate replacement of lost blood, and individual attention to tube drainage are points to emphasize as important to prevent complications. The eventual fate of a patient is more adversely affected by surgical complications than by any other single factor, and the avoidance of preventable surgical mishaps is of paramount importance.

Since July 1952, a good result has been obtained in over 90 per cent of patients operated upon, and in the same period 340 consecutive resections have been done without an early death. One patient died of surgical complications 6 months following his operation.

CONCLUSION

Utilizing long term chemotherapy, conservative operative approach, adequate postoperative bed rest, and drug therapy, a good clinical result should be obtained in 90 per cent or more of pulmonary resections for tuberculosis, and the mortality from the procedure should approach the minimum for all major surgery. Our experience indicates that there is no significant difference in the response to surgery between the negro and white races.

RUPTURE OF THE STOMACH IN THE NEWBORN INFANT

LESTER L. VARGAS, M.D., SHELDON M. LEVIN, M.D., and
THOMAS V. SANTULLI, M.D., F.A.C.S., New York, New York

RUPTURE OR PERFORATION of the stomach is a surgical emergency which is infrequently encountered in the neonatal period and too often the condition is not suspected until postmortem examination. Failure to consider the possibility results in a delay in diagnosis which contributes to the very high mortality even when surgical repair is attempted. If these babies are to be saved the perforation must be promptly recognized and repaired.

The first report of gastric perforation in a newborn infant was published by Siebold in 1825. In 1943, Herbut reviewed the literature and found 15 cases, to which he added 1 of his own. Five additional cases had been reported which did not appear in his series. Since then, 34 cases have been recorded bringing the total to 55 cases.

The first attempt to repair a gastric perforation in a newborn infant was reported by Stern and associates in 1929. Unfortunately, reperforation occurred 48 hours later and the infant succumbed. In 1932, Selinger successfully repaired a gastric perforation in a 3 month old baby, but it was not until 1950 that Légar reported the first newborn to survive the operation. In 22 recorded cases which were surgically treated, only 9 infants have survived (Table I).

From the Department of Surgery, College of Physicians and Surgeons, Columbia University, and the Surgical Service of the Babies Hospital, New York.

Eleven cases of perforation of the stomach in the newborn infant have been seen at the Babies Hospital of the Columbia-Presbyterian Medical Center since 1943. Closure of the perforation was performed in 8 patients; only 2 survived. Autopsies were performed on all infants who died except 1 who had been operated upon before. This communication is based on our experience with these 11 cases and on an analysis of 22 previously reported cases in which surgical repair was performed (Tables I, II, and Fig. 1).

PATHOGENESIS

Until 1943 all cases of perforation of the stomach in the newborn were attributed to acute or chronic peptic ulceration. Bird and his associates presented an excellent review of the voluminous literature concerning this disease in infants that had accrued since Cruveilhier's original description in 1829. While peptic ulcer is almost always the cause of duodenal perforation in infants, it accounts for fewer than one-half of the cases of ruptured stomach. In 1 of our cases (Case 6) several acute ulcers were found adjacent to the site of rupture and it is possible that the tear originated in one of them. Overwhelming septicemia with ulceration and necrosis of the stomach wall occurred in 2 other cases in our series (Cases 2 and 3). Craig and other authors have considered intracranial hemorrhage resulting from birth injury to be the

TABLE I.—SURGICALLY TREATED CASES SUMMARIZED FROM THE LITERATURE (22 CASES)

Author	*Date*	*Site and size of perforation*	*Presumed cause for perforation*	*Day of onset*	*Interval to operation, hrs.*	*Result*
Stern *et al.*	1929	Post. lesser curvature, ¼ in.	Acute ulcer	2	35	Reperforated and died
Dunham and Goldstein.	1934	Upper ½ of greater curvature, 1 cm.	Acute ulcer	4	9 days	Died
Smythe	1934	Lesser curvature, 2 perforations	Acute ulcers	6	17	Died, one ulcer not found
Quinn	1940	Ant.—close to cardia, 1.5 cm.	Acute ulcer	2	6	Died
Pendergrass and Booth.	1946	2 perforations, 1 and .5 cm on lesser and greater curvatures	Undetermined	3	?	Died
Burnett and Halpert	1947	Greater curvature, 2 cm.	Pyloric obstruction	1	19	Died
Gottlieb *et al.*	1950	Upper ½ of greater curvature, 3 cm.	Intracranial hemorrhage, acute ulcer	2	24	Died
Légar *et al.*	1950	Greater curvature	Acute ulcer	6	16	Survived
Kellogg *et al.*	1951	Post.—close to cardia, 2.5 cm.	Nasogastric tube?	4	12	Survived
Ross *et al.*	1952	Upper ½ of greater curvature, 4 cm.	Muscle defect	3	2	Survived
Sanford and McLendon	1952	Middle of greater curvature, 1 cm.	Meconium ileus	2	48	Died
Beattie and Bohan	1952	Prepyloric, lesser curvature, 3 mm.	Acute ulcer	3	15	Survived
Stein and Wright	1953	Greater curvature, 2.4 cm.	Undetermined	3	27	Died
		Greater curvature, 5 mm.	Undetermined	2	6	Survived*
		Upper ½ of greater curvature, 5 mm.	Undetermined	3	12	Died
Greene and Gose	1953	Greater curvature, 2 cm.	Acute ulcer	3	?	Died
Giannattasio *et al.*	1953	Upper ½ of lesser curvature, 2 cm.	Acute ulcer	4	15	Survived
Braunstein	1954	Upper ½ of greater curvature, 3 cm.	Muscle defect	5	?	Survived
Northway *et al.*	1954	Upper ½ of greater curvature, 2 cm.	Muscle defect	3	8	Survived
Foman *et al.*	1954	Upper ½ of stomach, 2 cm.	Idiopathic	2	48	Died
Wilson	1955	Lesser curvature, 5 cm.	Undetermined	3	?	Died
Arnold	1955	Ant.—close to greater curvature, 3 cm.	Undetermined	5	3	Survived

*Died 7 weeks after operation for intestinal obstruction.

TABLE II.—SUMMARY OF BABIES HOSPITAL CASES (1943–1955)

	Date	*Gastric intubation*	*Day of onset*	*X-ray*	*Interval to operation*	*Result*	*Cause of death*
Case 1. (706771) Male—full term Birth wt. 2,780 gms.	1943	None	6	Pneumoperitoneum	No operation	Died 20 hrs. after onset	Peritonitis
Case 2. (857549) Female—premature Birth wt. 2010 gms.	1947	None	2	Pneumoperitoneum	11 hrs.	Died 14 hrs. postop.	Hem. streptococcal septicemia, subarachnoid hemorrhage, and peritonitis
Case 3. (002295) Male—full term Birth wt. 2954 gms.	1950	None		Diagnosis not suspected	No operation	Died 3 days after onset	E. coli-aerogenes septicemia, and peritonitis
Case 4. (027903) Female—premature Birth wt. 820 gms.	1950	Gavage feeding on second day of life	4	Diagnosis not suspected	No operation	Died 24 hrs. after onset	Peritonitis and prematurity
Case 5. (032647) Female—premature Birth wt. 2,272 gms.	1951	Nasogastric suction immediately after operation*	15†	Hydropneumoperitoneum	24 hrs.	Died 2 days postop.	Peritonitis
Case 6. (050405) Male—premature Birth wt. 2,025 gms.	1951	None‡	2	Hydropneumoperitoneum	4½ hrs.	Reperforated and died	Peritonitis
Case 7. (080434) Female—premature Birth wt. 1,193 gms.	1952	Gavage feeding on second day of life	3	Hydroperitoneum, lipiodol localized site of perforation	48 hrs.	Died 5 days postop.	Peritonitis and prematurity
Case 8. (142291) Male—full term Birth wt. 2,900 gms.	1953	None	3	Pneumoperitoneum	14 hrs.	Died 34 hrs. postop.	Peritonitis
Case 9. (201065) Female—premature Birth wt. 1,900 gms.	1954	None	3	Pneumoperitoneum	9 hrs.	Survived	———
Case 10. (216936) Male—full term Birth wt. 3,180 gms.	1955	Gastric aspiration on first day of life	7	Pneumoperitoneum	6 hrs.	Died 9 days postop.	Intracranial hemorrhage, bilateral hydronephrosis (severe)
Case 11. (229356) Male—full term Birth wt. 3,200 gms.	1955	None	3	Pneumoperitoneum	6 hrs.	Survived	———

*Enteroenterostomy had been performed on the tenth day of life for atresia of the ileum.
†The fifth postoperative day (15th day of life) see*.
‡The infant was cyanotic at birth. Oxygen under 8 cm. of water positive pressure was administered.

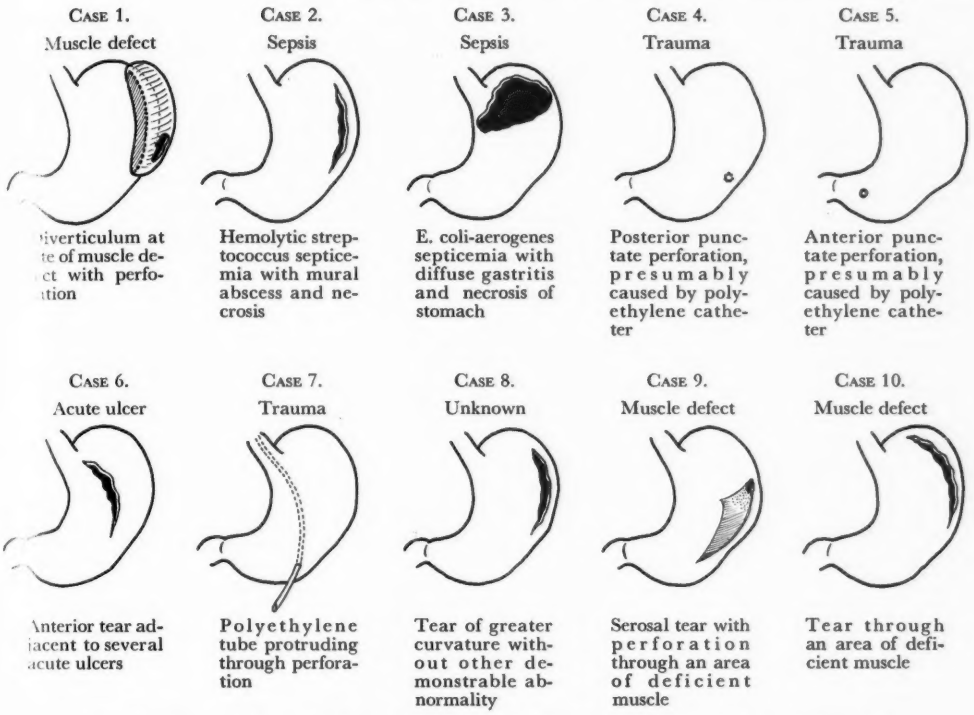


FIG. 1. Cause and location of perforations in Babies Hospital cases. (Case 11 is not shown. It is described in Table II.)

cause of gastric ulceration. Although evidence of intracranial bleeding was found in 2 of our 10 cases, it was not considered a factor contributing to the perforations.

Herbut in 1943 reported a case in which gastric rupture occurred through an area of congenital muscle deficiency. Ten additional cases of muscle deficiency have since been reported by Braunstein, Griffin and Griffin, Northway and associates, Potter, and Ross. All of these patients had tears varying from 2 to 6 centimeters in length along the fundic half of the greater curvature. Two cases of perforated gastric diverticulum were reported by Brody and by Stein and Wright. These probably represented a variant of the same anomaly since they were devoid of muscle, communicated with the gastric lumen through a long narrow neck, and were similarly situated high along the greater curvature. Proved congenital muscular defects accounted for rupture in 2 of our cases (Cases 1 and 10) (Fig. 2). The findings in Cases 9 and 11 (the infants who survived operation) strongly suggested a muscle deficiency and we have assumed that this was the cause.

In many of the reported cases no cause for the perforation could be determined after study of the postmortem material and the clinical record. Some were studied at autopsy after the perforation had been repaired, as in 1 of our cases (Case 8). However, the appearance and location of many of these suggest that some type of congenital muscle deficiency occurred with greater frequency than has heretofore been appreciated.

Abdominal trauma during delivery has been suggested as a possible etiologic factor by Greene and Gose, but a verified instance has never been reported. Since it is unusual

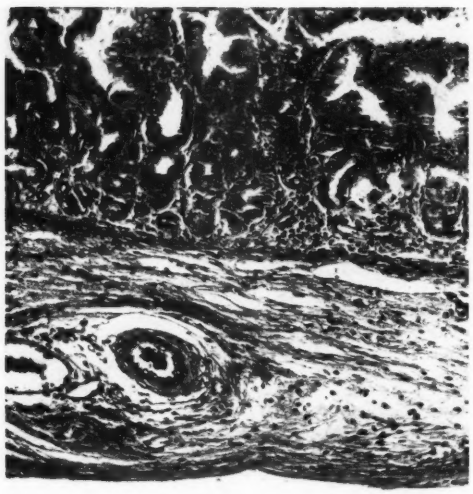


FIG. 2. Photomicrograph of a representative section of the full thickness of the stomach wall at the site of rupture. ×95. Note that between the mucosal and peritoneal surfaces no muscularis is seen.

for air to enter the gastrointestinal tract until after birth, compression within the birth canal would be unlikely to cause rupture of a small, nondistended viscus. We found no evidence in our series of trauma to the abdomen during delivery as a causative factor.

Rupture of the stomach resulting from distal obstruction in the gastrointestinal tract has been reported by Lee, Smythe, and others. The obstruction in these cases occurred at the duodenum, the pylorus, or the ileocecal valve. In Brody's case a proved muscle defect was found and in 3 others, rents in the fundus were described suggesting that obstruction in conjunction with some type of focal weakness accounted for the rupture. One of our patients (Case 5) with an atresia of the ileum had a gastric perforation on her fifteenth day of life, 5 days after resection and enteroenterostomy. Because of the appearance of the lesion and the fact that continuous nasogastric suction had been employed postoperatively, we considered the tube to be the cause. However, the possibility that distal obstruction contributed to the perforation could not be excluded.

Gastric perforation resulting from the use of a nasogastric tube for aspiration or gavage feeding in the newborn has been recorded by Kellogg, Potter, Wagner, and Wilson. Three of our perforations were thought to have been caused by a tube (Cases 4, 5, and 7). In 1 of these (Case 7) a beveled polyethylene tube was found protruding through the stomach wall. The evidence of minimal inflammation at the site of punctate perforations and a history of intubation in the other 2 cases seemed adequate to implicate the tube as the etiologic factor.

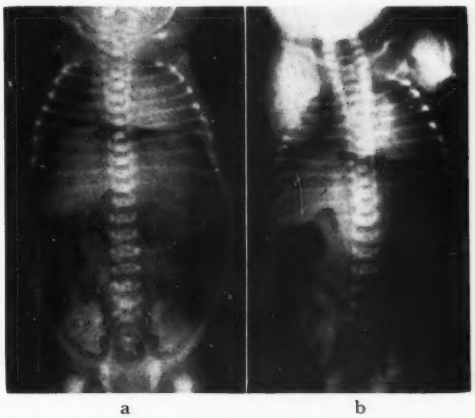
Six of the 10 cases in our series and over half of those previously reported were in premature infants. Since the incidence of prematurity is approximately 6 per cent of live-born infants, it would appear that the condition is more prevalent in the premature than in the full term infant.

DIAGNOSIS

The clinical picture is remarkably constant. Most of the infants appear normal at birth and oral feedings are usually well tolerated. However, a few of the babies have feeding difficulties and sometimes refusal of food may be the first indication of trouble. The stools are usually normal but may be bloody. Vomiting is inconstant and varies from regurgitation of small amounts of bile-stained fluid to frank hematemesis. Most gastric perforations occur within the first week of life, rarely later than 2 weeks. Abdominal distention usually appears suddenly. Although tense and tympanitic, the abdomen is soft. Liver dullness is absent. A paralytic ileus ensues and bowel sounds disappear. The severe abdominal distention limits diaphragmatic excursion so that dyspnea and cyanosis soon appear. Occasionally the sudden soiling of the upper abdominal peritoneum will cause diaphragmatic irritation. In these cases, rapid shallow respirations and cyanosis may be the first signs of the acute abdominal emergency. Efforts to relieve the distention by nasogastric suction are unrewarding, and failure to recover fluid used to irrigate the tube may suggest the

possibility of perforation. Dehydration and shock follow the loss of large amounts of extracellular fluid into the inflamed peritoneal cavity and distended bowel. In our experience, the blood count has only reflected the state of hydration and has not helped in making the diagnosis.

The diagnosis of a ruptured hollow viscus can be made in most instances by means of the plain upright x-ray of the abdomen. In four cases the roentgenogram was characteristic. The liver and spleen fell away from the elevated diaphragm, and the intervening space appeared as a radiolucent crescent. When a great deal of air was present some of the abdominal viscera were clearly outlined (Fig. 3). Free fluid gravitated to the lower abdomen, and a continuous fluid level traversing several distended intestinal loops was seen. Because neonatal perforations are frequently large and in the upper half of the stomach, the usual gastric bubble is absent. Free peritoneal air can easily be overlooked when a scout film is taken with the patient in the dorsal recumbent position. This is particularly true when there is free fluid in conjunction with a paralytic ileus. In 1 of our patients (Case 1), a flat film was read while still wet and interpreted as showing only an adynamic ileus. Efforts to decompress the gastrointestinal tract resulted in delay and the infant died before exploration could be performed. In another patient (Case 7) a fine polyethylene tube perforated the stomach and protruded into the free peritoneal cavity. Gavage feeding was continued and the abdomen was flooded with formula. Free air did not enter the peritoneal cavity since the tube fit the gastric defect snugly. The x-ray film in this case showed a diffuse ground glass density, characteristic of hydroperitoneum, and dilated intestinal loops. An accurate diagnosis was finally made by instilling lipiodol through the tube but only after a delay of 48 hours.



a b

FIG. 3. a, An upright plain roentgenogram of the abdomen demonstrating the subdiaphragmatic collection of air and the clearly outlined abdominal viscera. b, A lateral decubitus film showing the pneumoperitoneum.

SURGICAL CONSIDERATIONS

The abdomen should be explored promptly as soon as the diagnosis of a ruptured hollow viscus is suspected. Preoperatively, a soft nasogastric tube is passed to aspirate the remaining gastric contents and blood is drawn for typing and cross-matching. The saphenous vein is exposed anterior to the medial malleolus and cannulated with a small polyethylene catheter for the administration of fluids, during and after operation. The importance of proper supportive treatment with blood, appropriate electrolyte solution, oxygen, local and systemic antibiotics, and vitamin K cannot be overemphasized.

Local anesthesia is preferred in the acutely ill infant. A gauze nipple saturated with a 1 to 3 mixture of brandy and 10 per cent dextrose provides adequate sedation to complement local ½ per cent procaine infiltration of the abdominal wall. A long, midline incision or a paramedian, muscle retracting incision is used. As soon as the peritoneal cavity is entered trapped air under pressure is released and the tensely distended abdomen becomes flaccid. This makes exploration of the abdomen and subsequent closure of the wound a relatively simple procedure, without requiring deeper anesthesia for relaxation. Any free fluid is aspirated and a specimen is taken for culture and sensitivity

studies. Because many tears occur close to the cardia, a particularly careful search of this region must be made. Division of the gastrocolic omentum will permit inspection of the posterior aspect of the stomach.

The perforation is repaired in two layers; the first a continuous through-and-through suture of fine chromic catgut swedged on an atraumatic needle, followed by an inverting layer of interrupted seromuscular sutures of fine silk. It is important to include only healthy gastric wall throughout the suture line even if this requires excision of the necrotic edge of the perforation. One of our patients (Case 6) reperforated when the suture line tore at the site of an acute ulcer. Following repair, the stomach is filled with warm sterile saline instilled through a soft rubber nasogastric tube in order to test the security of the closure, discover other perforations, and exclude the possibility of distal obstruction. The peritoneal cavity is then thoroughly irrigated with warm sterile saline and a local antibiotic (a solution of neomycin and bacitracin) is instilled. Drainage is ordinarily not employed unless there is an abscess or a question of insecure closure. In those cases a soft Penrose drain is placed down to but not against the repair. Continuous low pressure nasogastric suction is used for 48 to 72 hours after operation and then small amounts of glucose water are given orally. The general supportive care is that used for any newborn infant undergoing major surgery.

RESULTS

One patient died before operation was performed and 2 others died without the diagnosis being suspected. In 8 patients, the perforation was repaired. Only 2 patients survived, a 1,900 gram premature female and a full-term male infant. Both patients are asymptomatic and doing well 7 months and 4 weeks after operation respectively. The causes of death are shown in Table II. One baby reperforated and died of peritonitis. Delayed diagnosis resulting in overwhelming peritonitis accounted for the death in 2 others. Although peritonitis was a factor in all the cases, prematurity, sepsis, and severe bilateral hydronephrosis associated with intracranial hemorrhage were the causes of death in the remaining 3 patients.

DISCUSSION

Rupture of the stomach in the newborn infant is an acute surgical emergency which must be promptly recognized and treated if more of these babies are to be saved. The prognosis depends upon the time elapsing between the onset of the catastrophe and operation in most cases. The diagnosis is not difficult to make if the possibility of a ruptured hollow viscus is considered in any newborn who is distended and dyspneic in the first week of life. A plain upright film of the abdomen will usually establish the diagnosis of pneumoperitoneum. This can only be due to perforation of the stomach, small intestine, or colon and requires early operation. Efforts to delineate precisely the site of the perforation with contrast media are rarely indicated and serve only to delay surgical intervention. One-half of the cases reported since Stern and his associates first attempted surgical repair in 1929 proved fatal without the diagnosis being suspected. With increasing awareness of the entity, 14 of the 16 patients reported in the last 5 years have come to operation and 9 of these have survived.

While it is conceivable that small gastric perforations might become quickly sealed and heal spontaneously, a verified instance has never been reported. In 1936 Tunger described a case of spontaneous pneumoperitoneum in a 5 day old infant. The baby continued to thrive and operation was deferred. Eighteen days later the peritoneal air was reabsorbed and the site of the perforation was never ascertained. Many of the infants are desperately ill when first seen, and it is tempting to consider treating them conservatively with continuous nasogastric suction. This technique is sometimes successfully employed in the management of perforations in adults who are poor opera-

tive risks. However, the omentum of the infant is poorly developed and in most instances the gastric perforations are relatively large. For these reasons, it is unlikely that spontaneous walling-off can occur and the infant's best chance for survival rests with immediate closure of the tear.

We have been impressed with the marked improvement in respirations after release of the tension pneumoperitoneum when the peritoneal cavity was opened at operation. Although we have not used preoperative paracentesis, it might help in selected cases.

The operation is not difficult and in most cases can be performed under local anesthesia. However, certain precautions deserve special consideration. The perforations extend over a large area of the relatively small infant stomach, and there is a tendency to fear compromising the lumen by either excising the necrotic edge or by turning in too much gastric wall. Unless the sutures are placed through healthy tissue there is danger of their tearing out. Reperforation occurred in 1 of our cases and a similar complication was reported by Stern and his associates. Care must be taken not to overlook multiple perforations. Smythe and Pendergrass and Booth have reported cases in which perforation occurred at two separate sites. Congenital muscle defects may also be multiple as observed by Braunstein and by Herbut. Obstruction of the intestinal tract must also be excluded before closing the abdomen since it is associated with rupture of the stomach in approximately 12 per cent of the reported cases.

The mortality for rupture of the stomach in newborns is inordinately high and is complicated by factors such as prematurity, serious associated anomalies, septicemia, and intracranial hemorrhage. However, peritonitis remains the most common cause of death in our series and in the cases studied from the literature. Since delay in diagnosis is a major contributing factor an increased awareness of this condition in the neonatal period should appreciably improve the salvage of these unfortunate infants.

SUMMARY

Fifty-five cases of gastric perforation in newborn infants have been previously reported. Twenty-two cases in which surgical repair was attempted are reviewed. Nine infants survived operation.

Our experience with 11 cases is presented. Closure of the perforation was performed in 8 patients; 2 survived.

Gastric ulcer accounts for perforation in less than one-half the cases while congenital muscle defects occur with greater frequency than has previously been appreciated.

The condition appears to be more prevalent in premature infants and usually occurs within the first 2 weeks of life.

The diagnosis is not difficult to make if the possibility of a ruptured viscus in the neonatal period is kept in mind.

Prompt surgery offers the only hope for survival in these babies.

REFERENCES

1. Arnold, G. G. Perforation of the stomach in the neonatal period. Report of a survival in a premature infant. J. Pediat., S. Louis, 1955, 46: 276.
2. Beattie, J. M., and Bohan, K. E. Perforation of gastric ulcer in premature newborn with operation and survival. Am. Surgeon, 1952, 18: 1146–1149.
3. Bird, C. E., Limper, M. A., and Mayer, J. M. Surgery in peptic ulceration of stomach and duodenum in infants and children. Ann. Surg., 1941, 114: 526–542.
4. Braunstein, H. Congenital defect of the gastric musculature with spontaneous perforation. J. Pediat., S. Louis, 1954, 44: 55–63.
5. Brody, H. Ruptured diverticulum of the stomach in a newborn with a congenital membrane occluding the duodenum. Arch. Path., Chic., 1940, 29: 125–128.
6. Burnett, H. A., and Halpert, B. Perforation of the stomach in a newborn infant with pyloric atresia. Arch. Path., Chic., 1947, 44: 318–320.
7. Craig, J. Quoted by Gellis, S. S. The Year Book of Pediatrics. P. 215. Chicago: Year Book Publishers Inc., 1954–1955.
8. Cruveilhier, J. Maladies de la bouche, de l'oesophage et de l'estomac. Anatomie pathologique du corps humain—Atlas. Vol. 1, Book 15, Plate 3, Figs. 4–6. Paris: J. B. Baillière, 1829.
9. Dunham, E. C., and Goldstein, R. M. Rupture of stomach in newborn infants. J. Pediat., S. Louis, 1934, 4: 44–50.
10. Fomon, S. J., Lowe, G. H., and DeLeeuw, H. Idiopathic rupture of the stomach in a newborn infant. Am. J. Dis. Child., 1954, 88: 234–238.
11. Giannattasio, R. C., Pirozzi, J. M., and Mullin, L. S. Perforation of the stomach in the neonatal period. N. York State J. M., 1953, 53: 2872–2874.
12. Gottlieb, C., Chu, F., and Sharlin, H. S. Perforation of a gastric ulcer associated with intracranial

hemorrhage in a newborn infant. Radiology, 1950, 54: 595–597.
13. Greene, W. W., and Gose, D. F. Perforation of the stomach in the newborn. Am. J. Dis. Child., 1953, 85: 47–51.
14. Griffin, J. P., and Griffin, C. G. Perforation of stomach in a newborn due to a congenital defect; a case report. J. Indiana M. Ass., 1954, 47: 619–621.
15. Herbut, P. A. Congenital defect in the musculature of stomach with rupture in the newborn infant. Arch. Path., Chic., 1943, 36: 91–94.
16. Kellogg, H. G., Abelson, S. M., and Cornwall, F. A. Perforation of the stomach in newborn infant. J. Pediat., S. Louis, 1951, 39: 357–362.
17. Lee, W. E., and Wells, J. R. Perforation in utero of a gastric ulcer. Ann. Surg., 1923, 78: 36–41.
18. Légar, J. L., Ricard, P. M., Léonard, C., and Piette, J. Ulcère gastrique perforé chez un nouveau-né avec survie. Union méd. Canada, 1950, 79: 1277–1280.
19. Northway, R. O., DeLano, R. H., and Claytor, A. A. Perforation of the stomach in the newborn infant; a case report. Surgery, 1954, 35: 925–927.
20. Pendergrass, E. P., and Booth, R. E. Report of a case of ruptured stomach in an infant three days old. Am. J. Roentg., 1946, 56: 590–593.
21. Potter, E. L. Pathology of the Fetus and Newborn. Pp. 295–296. Chicago: Year Book Publishers Inc., 1952.
22. Quinn, A. G. Report of two ruptured gastric ulcers and one ruptured duodenal ulcer in three newborn infants. South. M. J., 1940, 33: 1171–1173.
23. Ross, M., Hill, P. S., and Hass, C. M. Neonatal rupture of the stomach. J. Am. M. Ass., 1951. 146: 1313–1314.
24. Sanford, M. C., and McLendon, P. A. Rupture of the bowel in a newborn infant, Clin. Proc. Child. Hosp., Wash., 1952, 8: 165–172.
25. Selinger, J. Peptic ulcer in infants under one year of age. Ann. Surg., 1932, 96: 204–209.
26. Siebold. Cited by Thiele, P.: Ueber Geschwuersbildungen des Gastro-duodenal-tractus im Kindesalter, Erg. inn. Med. Kinderh., 1919, 16: 302–383.
27. Smythe, F. W. Gastric ulcers in premature newborn. Am. J. Surg., 1934, 24: 818–826.
28. Stein, F. E., and Wright, L. T. Rupture of hollow and solid viscera in the newborn. Harlem Hosp. Bull., 1953, 6: 32–57.
29. Stern, M. A., Perkins, E. L., and Nesse, N. S. Perforated gastric ulcer in a two day old infant. Lancet, Lond., 1929, 49: 492–494.
30. Tunger, H. Spontan pneumoperitoneum bei einem neugeborenen. Mschr. Kinderh., 1936, 67: 264.
31. Wagner, E. A., Jones, D. V., Koch, C. A., and Smith, D. C. Polyethylene tube feeding in premature infants. J. Pediat., S. Louis, 1952, 41: 79.
32. Wilson, M. G. Abdominal surgery in the newborn. Surg. Gyn. Obst., 1955, 100: 141–148.

BRONCHOGRAPHY WITH DIONOSIL

G. C. JOYNT, M.D., F.A.C.S., F.R.C.S. (Can.), and

L. HARNICK, M.D., Toronto, Canada

DIONOSIL IS A NEW CONTRAST MEDIUM that has been developed for bronchography. It is an aqueous suspension of a radiopaque substance of low solubility and differs fundamentally from previous contrast media which have been either oily iodides or aqueous solutions. Since the introduction of 40 per cent iodized poppy seed oil by Sicard and Forestier in 1922, many new contrast media have been produced in an attempt to eliminate the disadvantages of lipiodol.

Bronchography is a procedure that is generally considered to entail little risk. The hazards with lipiodol are: (1) an untoward reaction to iodine, which although rare, is well recognized and may be serious; (2) local tissue granulomatous reactions which may result with lipiodol and persist. The most annoying feature of lipiodol is, however, the persistence of the material in the alveoli roentgenographically long after its instillation. This may obscure the pathologic lesion as noted in serial roentgenograms.

In 1948, umbradil (diodone or diodrast in a carboxymethyl cellulose base) was introduced and was used enthusiastically by many clinicians. It disappears roentgenographically in a few days but at the Toronto Western Hospital it was found to be too irritating to the bronchial mucous membrane and was discontinued. In February 1952, when dionosil was introduced into Canada, it was tried first at the Toronto Western Hospital and at the Thoracic Unit in Sunnybrook Department of Veterans Affairs Hospital in Toronto. In this preparation the iodine is in organic combination and there is no breakdown of free iodine or inorganic iodides which might be capable of causing delayed effects. With dionosil there is, therefore, no risk of iodism. Clinically, we have had no experience with "dionosil oily," which has the disadvantage of an oily base but is slightly less irritating to the bronchial mucous membrane. Nevertheless, it still has the disadvantage of an oily base with the possibility of granulomas being produced in the lung. If an intratracheal catheter is used for instillation of the aqueous suspension, it has proved not to be too disturbing to the patient.

From the Toronto Western Hospital and the University of Toronto Medical School. Supported in part by a grant from the Banting Research Foundation.

Dionosil is a 50 per cent suspension of an ester closely related to diodrast or diodone as it is known in England. It is available in two forms: (1) An aqueous suspension, which is 50 per cent weight per volume of the propyl ester of 3:5 diiodo-4-pyridone-N-acetic acid (propyliodone) in water with the aid of sodium carboxymethyl cellulose. Sodium citrate is present as a buffer and the preparation is rendered isotonic with sodium chloride. A small portion of benzyl alcohol is used as a bacteriostatic agent. (2) Dionosil oily which is a 50 per cent weight per volume suspension of the same substance in pure arachis oil.

The most important advantage of dionosil is its rapid elimination from the lungs in 3 or 4 days so that plain roentgenograms are not obscured. It appears to be well tolerated by the patient and is nontoxic. Occasionally, there is a febrile reaction which lasts 24 to 48 hours but it has been used in active tuberculosis without untoward incident.

The toxicity of dionosil in the tracheobronchial tree has been studied in rabbits by Tomich, Basil, and Davis. Local anesthesia was not used as it would depress the cough reflex which serves as an indication of the degree of irritation produced. As anticipated, it was found that the aqueous suspension was somewhat more irritating than

TABLE I.—DIONOSIL BRONCHOGRAMS IN RESIDENT PATIENTS

	No.
No. of patients	85
No. of examinations	129
No reaction	79
Slight reaction	37
Moderate reaction	13

the oily dionosil. With the aqueous suspension, macroscopic signs of irritation in lungs of rabbits became apparent in 16 hours and reached a maximum at 3 days. After 2 weeks the lungs appeared normal. In no animal could sodium carboxymethyl cellulose be demonstrated after 5 days. Excretion studies in rabbits were carried out by labelling the compound with I^{131}. When given by the intratracheal or oral routes the urinary excretion rate showed a minimum of 95 per cent recovery in 72 hours. It would appear that the propyliodone is hydrolyzed in the bronchial tree and the resultant organic anion is then rapidly removed by the kidney. Since neither iodine nor iodide ion could be detected in the urine after intratracheal or oral administration, if follows that it should be possible to administer the material to iodine-sensitive patients. Recently, 2 cases of sensitivity to dionosil were reported.

Since February 1952, aqueous dionosil has been used for bronchograms as well as injection of fistulas and sinuses at the Toronto Western Hospital. Over 900 bronchograms have been carried out. Frequently there were 2 separate examinations of a patient and in 8 patients more than 3 examinations were carried out with this medium. In only 2 patients was there a moderately severe reaction with bronchospasm and chills and in 1 case, fever to 102 degrees. Most of the examinations were done on out-patients, but in a review of 85 in-patients who had 129 examinations, there was little or no reaction in 116 examinations and the remaining 13 showed fever over 100.5 degrees up to 48 hours (Table I).

TABLE II.—BRONCHOGRAMS IN DOGS

	Sacrificed			
	4 days	*7 days*	*14 days*	*28 days*
Lipiodol	2	2	2	4
Dionosil	2	3	3	6
"Dionosil oily"	2	2	2	9
Propyliodone				4

The medium outlines the bronchial tree clearly through the formation of a coating of material on the mucous membrane rather than bronchial filling and does not produce alveolar filling (Fig. 1). The lung fields and tracheobronchial tree are roentgenographically clear in 3 or 4 days. In view of the rapid clearing of the lung fields, it has been suggested that operation need not be delayed following a dionosil bronchogram. With lipiodol it has been our custom to delay 3 to 6 weeks in order that most of the oil is eliminated and the local tissue reaction in the lung has subsided. Weinberg has demonstrated that large amounts of iodized oil instilled intrabronchially produce atelectasis and nonspecific pneumonitis. Gowar and Gilmour have demonstrated in animals the granulomatous reaction that may result with lipiodol. This reaction has also been shown by Felton, Wright, and others in human surgical specimens.

An experimental study of dionosil and lipiodol bronchograms has been carried out in dogs, as a Banting Research Foundation project at the University of Toronto.

MATERIAL AND METHODS

Apparently healthy mongrel dogs, weighing 8 to 10 kilograms, were employed for this study. The anesthetic induction consisted of an intravenous injection of nembutal, 35 milligrams per kilogram of body weight and an x-ray film was made of the chest before the bronchogram was carried out. Under fluoroscopy, the material (dionosil or lipiodol) was instilled through a bronchoscope into the main stem bronchus and the branches were filled by posturing the animal. Immediately after the bronchogram, a roentgenogram was done to check for adequate filling and the animals were sacrificed at intervals of 4, 7, 14, and 28 days. Figure 2a shows a dog with dionosil bronchogram, and recheck roentgenogram 4 days later (Fig. 2b) shows the opaque material entirely disappeared.

FIG. 1. Normal human bronchogram.

A total of 45 bronchograms were carried out on 43 mongrel dogs. In 4 animals, lipiodol and dionosil bronchograms were done simultaneously, but death occurred in 2 animals in 1 and 4 days respectively. Subsequently, the bronchograms were carried out in one lung, using the normal side as control.

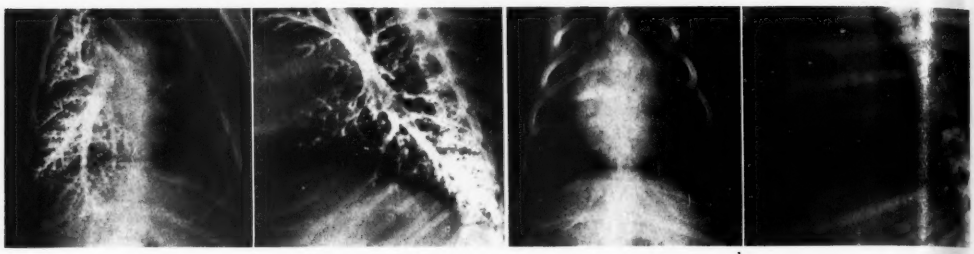
An arbitrary quantity of 5 cubic centimeters of lipiodol or 10 cubic centimeters of dionosil was used to fill one lung. This amount gave satisfactory filling of the entire bronchial tree on one side. (The usual quantity in adult human bronchograms is 10 cubic centimeters of lipiodol and 15 to 20 cubic centimeters of dionosil for each lung.) In 4 animals, the effect of N propyl 3:5 diiodo-4-pyridone-N acetate (propyliodone) suspended in 20 cubic centimeters of water with 3 minims of polyethylene glycol was observed.

When the animals were sacrificed, an intravenous anesthetic of nembutal was given and the trachea exposed in the neck. Immediately after a lethal dose of anesthetic was injected, the trachea was clamped with forceps and the trachea, heart, and lungs were removed en masse. The gross and microscopic features of the injected lungs, as well as the normal lungs, were studied.

RESULTS

As shown in Table II, a comparative study of dionosil, dionosil oily, and lipiodol bronchograms was carried out. In addition, 4 animals had propyliodone in water injected into one lung and were sacrificed at 28 days.

In the lipiodol and dionosil animals, there was a moderately acute inflammatory response in the lung, at the end of 1 week (Figs. 3 and 4). This gradually lessened over a period of 4 weeks, and at the end of 28 days the 6 dionosil animals showed relatively normal lungs, both grossly and microscopically. One of the 4 lipiodol animals sacrificed



a b

FIG. 2. a, Dionosil bronchogram in dog. b, Roentgenograms 4 days later.

at the end of 28 days demonstrated a typical foreign body granuloma (Fig. 5) similar to the lung sections demonstrated by Felton in human surgical specimens. In 9 animals with dionosil oily only 2 showed a relatively normal lung and the remainder showed patchy atelectasis grossly and microscopically. There were foreign body granulomatous changes in most of the specimens and in 2 specimens there was an active fibroblastic proliferation with complete destruction of normal lung in many areas (Fig. 6a and b).

In the 4 animals in which propyliodone and water were used, the lungs appeared relatively normal. Zollinger and Fischer studied the effects of carboxymethyl cellulose in 100 human surgical specimens obtained by lobectomy or pneumonectomy, and in this group 5 cases showed a remnant of the carboxymethyl cellulose in the diseased areas. In 2 of their specimens, no granulomas were found, but there were phagocytes surrounding masses of carboxymethyl cellulose in the alveoli. In 2 other specimens, a few small granulomas with giant cells were found, and in 1 case there was moderately severe damage to lung tissue of the lingula with granulomatous formation. That, it was believed, was due to flooding of the alveoli with the injection medium. Their experimental observations on rabbits revealed no evidence of retention of carboxymethyl cellulose when the tracheobronchial tree alone was filled, but when there was massive alveolar filling there was retention of carboxymethyl cellulose which lasted several weeks and was followed by granulomatous reaction in the lung. They concluded that the carboxymethyl cellulose could cause granulomas but that it rarely did so, except

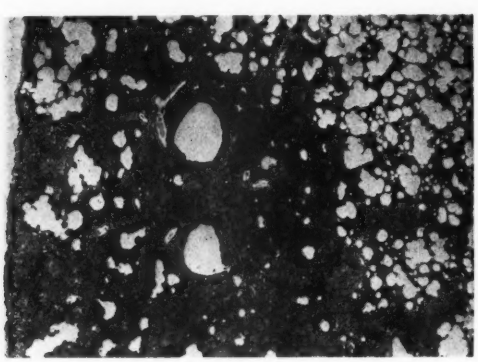


FIG. 3. Pathologic changes in dog's lung 7 days following a lipiodol bronchogram. There is a moderate degree of interstitial pneumonia with characteristic granulomas in the perivascular and peribronchial area. × 13.

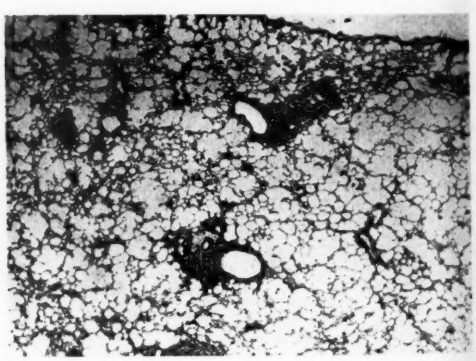


FIG. 4. Pathologic changes in dog's lung 7 days following a dionosil bronchogram. A granulomatous reaction about the bronchi with an occasional foam cell in the peribronchial region. × 13.

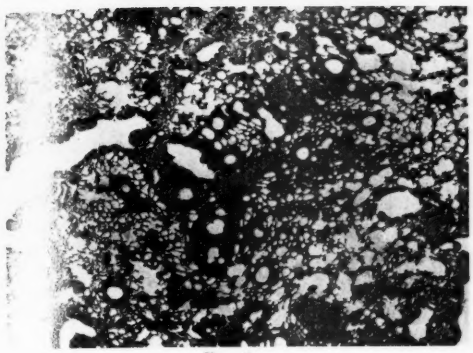
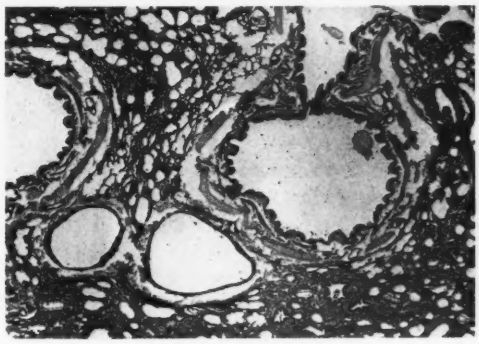
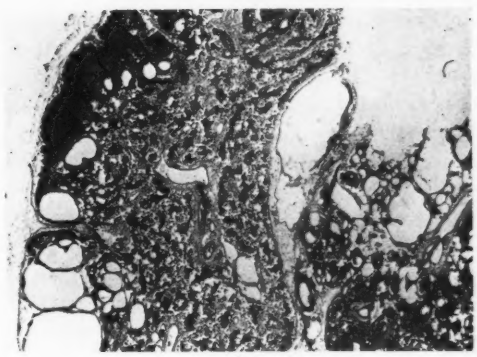


FIG. 5.

5. Pathologic changes in dog's lung 28 days following lipiodol bronchogram. Typical foreign body granulomas surrounding lipiodol droplets. × 13.



a



b

FIG. 6.

6. a, Pathologic changes in dog's lung 28 days following "dionosil oily" bronchogram. Diffuse fibrosis with granulomas and giant cells. There are large air spaces filled with oil which are surrounded by granulomas and giant cells. b, Hilar node in the same animal, which shows moderately severe granulomatous lymphadenitis with large spaces full of oil with granulomatous reaction and giant cells around the spaces. × 13.

in those cases in which there had been massive bronchial and alveolar filling.

DISCUSSION

Dionosil is a new contrast medium which appears to offer some advantages over lipiodol in bronchography. It would appear from experimental data that the aqueous suspension, although somewhat more irritating than dionosil oily, produces less reaction in the lung. It has been suggested that lung resection need not be delayed following a bronchogram with dionosil but the results in dogs suggest that 3 to 4 weeks should elapse before segmental or lobar resection of the lung is carried out. In 1 patient, in whom a segmental resection was done for chronic tuberculous bronchiectasis a week after bronchography with dionosil, the microscopic section showed widespread granulomatous reaction which suggested active tuberculosis. We now delay resection for 3 to 4 weeks following bronchography.

From our experimental observations, there appears to be more evidence of patchy atelectasis and granulomatous reaction with dionosil oily bronchograms, and there appears to be a greater tendency for alveolar filling. It offers, however, the advantage of being somewhat less irritating to the mucous membrane, but with good topical anesthesia there has been little discomfort from the aqueous preparation.

SUMMARY AND CONCLUSION

The effect of dionosil and dionosil oily bronchograms has been studied in dogs. Dionosil, an isotonic suspension of 50 per cent weight per volume of the propyl ester of 3:5 diiodo-4-pyridone-N-acetic acid in

water in a sodium carboxymethyl cellulose base, produces a coating on the bronchial wall which clearly outlines the bronchial tree, with little or no alveolar filling. No granulomatous reaction has been noted in the lungs of dogs at the end of 4 weeks, with the aqueous suspension. Clinically, it appears to be well tolerated in adults and is nontoxic, although there may be slight febrile reaction lasting 24 to 48 hours. It may be used in active tuberculosis without danger. Patients sensitive to iodine or iodized oils do not react to dionosil as no free iodine or iodides are liberated.

REFERENCES

1. Felton, W. L. The reaction of pulmonary tissue to lipiodol. J. Thorac. Surg., 1953, 25: 530.
2. Gowar, F. J. S., and Gilmour, J. R. Changes in lung following injections of iodized oil into trachea. Brit. J. Exp. Path., 1941, 22: 262.
3. Tomich, E. G., Basil, B., and Davis, B. A report on the properties of n-propyl 3:5-di-iodo-4-pyridone-N-acetate (propyliodone). Brit. J. Pharm.,1953, 8: 166.
4. Weinberg, J. A. Iodized oil in bronchiectasis including study of 2 cases following lobectomy. Arch. Surg., 1933, 27: 545.
5. Wright, R. D. Reaction of pulmonary tissue to lipiodol. Am. J. Path., 1935, 11: 497.
6. Zollinger, H. U., and Fischer, F. K. Weitere empirische und experimentelle Untersuchungen ueber die Joduron-Bronchographie. Schweiz. med. Wschr., 1953, 83: 645.

BENEFICIAL ACTION OF PRETREATMENT WITH CHLORPROMAZINE ON SURVIVAL FOLLOWING GRADED HEMORRHAGE IN THE RAT

S. G. HERSHEY, M.D., I. GUCCIONE, B.S., and B. W. ZWEIFACH, Ph.D.,
New York, New York

A NUMBER OF RECENT STUDIES concerned with the shock syndrome have dealt with methods of protecting experimental animals against the deleterious effects of severe stress. Investigations of Fine (4), Baez (2), Remington (9), and of this laboratory (7) indicate that protection against otherwise lethal injury is a valid and predictable entity. Protection has been induced in the presence of a variety of stress situations such as trauma, hemorrhage, infections, and x-radiation. Experimental methods reported as generating protection are varied and appear to have no obvious factor(s) common to each. In general, protection of this type against stress seems to be the result of an altered response to injury rather than to a modification or attenuation of the stress per se.

The present study with chlorpromazine was undertaken because of the resemblance of this drug to another effective protective agent, dibenzylene, in being an autonomic blocking drug with adrenolytic properties and in its specific effects on vascular mechanisms. Chlorpromazine is also a principal component of the "lytic cocktail" utilized for artificial hibernation, a procedure empirically claimed by Laborit (8) and others to protect subjects against the unfavorable effects of injury and extensive surgical procedures. Despite the extensive clinical use of this drug, data relating to its precise relationship to mechanisms of protection are speculative.

From the Department of Anesthesiology, New York University Postgraduate Medical School, the Joseph and Helen Yeamans Levy Laboratory of Beth Israel Hospital, and the Department of Biology, Washington Square College of Arts and Sciences, New York University.

This study was aided by a research grant (H-1244) from the National Heart Institute, National Institutes of Health, U. S. Public Health Service.

Preliminary studies with chlorpromazine in this laboratory indicate that it is an effective protecting agent (6). The drug is capable of eliminating or attenuating many of the decompensatory vascular phenomena associated with the irreversible phase of the shock syndrome produced by trauma and hemorrhage.

This report represents an experimental appraisal of the capacity of chlorpromazine to protect animals subjected to several grades of hemorrhagic hypotension. It is also an attempt to identify some of the stigmas characteristic of the protected state in animals.

The results indicate that pretreatment with chlorpromazine affords a significant degree of protection against hemorrhagic hypotension, up to the point where the hypotensive episode becomes extremely severe. Protected animals, when compared with controls, show significant differences relative to the manner in which they require and respond to blood administration, and to the absence of gross visceral lesions associated with irreversible shock.

METHODS

Wistar strain female rats, 50 to 60 days old, were used. The animals were divided into five groups according to the bleeding pattern to which they were subjected. Experiments were done in pairs within each group, with one member of the pair serving as control.

Group 1. Blood loss and take-up adjusted to maintain a mean blood pressure of 75 millimeters of mercury for 2 hours.

Group II. Blood pressure maintained at 50 millimeters for 2 hours.

Group III. Blood pressure maintained at 65 millimeters for 1 hour followed by 2 hours at 50 millimeters.

Group IV. Blood pressure adjusted to 50 millimeters for 3 hours.

Group V. Blood pressure maintained at 65 millimeters for 1 hour followed by 2 hours at 40 millimeters.

The bleeding patterns represented progressively severe and prolonged grades of hemorrhage. Bleeding was accomplished through a cannulated carotid artery leading to a conventional mercury manometer and a previously described (1) spontaneous bleed-out take-up reservoir filled with heparinized saline. This device permits reliable maintenance of preselected blood pressure levels with precise control and measurement of bleed-out and take-up blood volumes. Intramuscular sodium pentobarbital anesthesia was used, 3.5 milligrams per 100 grams body weight for controls and 2.0 milligrams per 100 grams for treated animals.[1] Chlorpromazine, 2.5 milligrams per 100 grams body weight, was given intramuscularly 30 minutes prior to injection of the anesthetic. Control animals received equivalent volumes of normal saline. This was the dose of chlorpromazine established as offering maximal survival against otherwise lethal trauma and drumming. Blood loss and reinfusion aliquots were achieved in graded steps and not abruptly. Only animals surviving the entire experiment were included in these data. In 9 of the controls and 7 of the experimental animals it was necessary to perform tracheotomy because mucous secretions developed. A permanent polyethylene tracheotomy tube was inserted and aspirated intermittently as required. The animals were returned to specially prepared cages to prevent occlusion of the tracheotomy tube. At the end of the hypotensive period each animal received by graded infusion the remainder of the blood in the reservoir. At this point the artery was ligated, the incision closed, and the animal returned to its cage for observation. Rats which were alive 24 hours after completion of the experiment were designated as survivors. Rats dying between the end of surgery and the twenty-fourth hour were labeled fatalities. Gross autopsies were routinely performed with particular attention to the liver, bowel, lungs, and kidneys.

[1]Chlorpromazine treated rats develop with the reduced dose of sodium pentobarbital a degree of narcosis equivalent to that obtained in controls.

RESULTS

Figure 1 represents typical protocols of paired individual experiments in chlorpromazine treated and control rats in group IV. The record for each animal indicates blood pressure levels, the volume of blood lost into the reservoir (plotted as per cent of body weight), the volume of blood spontaneously taken up from the reservoir during the latter phase of the hypotensive period, the reinfusion of blood remaining in the reservoir at the end of the period of hypotension, the 24 hour survival or death, and capsule gross autopsy findings. A total of 143 experiments are reported in which 75 are control and 68 chlorpromazine treated animals. Although not included in these data, it is of interest to note that among the animals which died during the acute part of the experiment and were therefore excluded from the total number of valid experiments, 41 were controls and only 13 chlorpromazine treated rats.

The bleed-out values represent a labile, self-adjusting blood loss sufficient to lower the blood pressure and to maintain it at the preselected level. Spontaneous take-up values also represent a self-adjusting volume of blood required to sustain the desired hypotensive level. During the hypotensive episode, according to the criteria of Fine and Seligman (5), the point at which the take-up phase supersedes the bleed-out phase is indicative of the onset of vascular decompensation and the progressive deterioration of the circulatory adjustments to hemorrhage. The

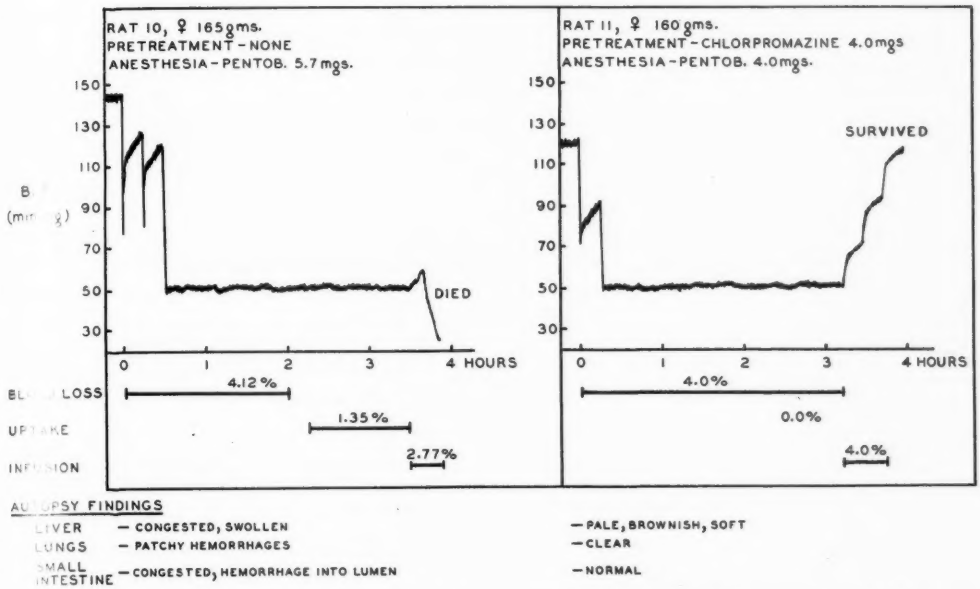


FIG. 1. Graded hemorrhage in rat. Protocols of paired experiments in chlorpromazine treated control rats in group IV. Blood loss, uptake, and infusion are indicated as per cent of body weight. Note the absence of spontaneous "uptake" of blood, the prompt, sustained response to blood replacement, and the absence of congestion and hemorrhage in the viscera in the chlorpromazine treated rat.

volume of blood taken up is an index of the degree of vascular decompensation and thereby is a measure of the magnitude of the physiologic stress to which the animal has been exposed.

Tables I to V summarize the data for the five groups of experiments comparing chlorpromazine treated rats with control animals. As indicated, survival rates for all untreated animals ranged from 33.3 to 58.3 per cent. Contrary to what might be anticipated among the controls, survival did not parallel the degree of hemorrhagic stress as graded from groups I to V, being 58.3, 42.8, 33.3, 56.0, and 43.0 per cent respectively. Survivors in control experiments showed maximum blood output values somewhat larger than the controls that died. By contrast, survival percentages for chlorpromazine treated animals in groups I to IV were consistently higher, ranging from 85.6 to 91.6 per cent with no apparent relationship to the intensity of hemorrhagic procedure. Survival of the drug treated rats in group V, the severest bleeding pattern, was only 52 per cent as compared with 43 per cent in the controls of this group. Since the differences were not statistically significant in this fifth group, a protective action of chlorpromazine was questionable.

In all five control groups, survivors showed a maximum blood output volume greater than that observed in controls which died. A difference in maximum blood loss between survivals and deaths was also observed in chlorpromazine treated rats with the exception of group I, the least severe bleeding procedure.

Differences in the spontaneous take-up of blood in both controls and treated animals were quite striking. Survivors in the control group consistently took up less blood than those which died. This difference in take-up volumes, although consistent, was not as marked in the drug-treated rats. In the chlorpromazine treated rats, the observation of

TABLE I.—EFFECT OF CHLORPROMAZINE IN HEMORRHAGIC STRESS IN GROUP I

	Controls	*Chlorpromazine**
No. of rats	12	12
Survivals, per cent	(7/12) 58.3	(11/12) 91.6
†Blood output survivals	3.27	1.86
Blood output deaths	3.05	3.58
‡Blood take-up survivals	0.03	0.01
Blood take-up deaths	0.56	0.00

*Thorazine (SKF) 2.5 mgm./100 gm. body wt.
†Average maximum blood loss indicated as per cent body wt.
‡Average maximum blood take-up indicated as per cent body wt.

special interest in regard to blood take-up was the small absolute values of this phenomenon. Treated survivors required little or no blood from the reservoir to sustain the blood pressure at selected levels.

A number of other observations were pertinent. Protected animals, throughout the period of hypotension, showed more favorable respiratory movements than controls. Their breathing was not as rapid and irregular. Furthermore, their skin, as noted in the ears and digital webs, was not cyanosed and congested but appeared pale and pink with a sustained emptying and refill capacity of the superficial vessels in response to mechanical pressure. Gross autopsy of fatalities revealed a marked congestion of the liver, spleen, and small intestine with considerable hemorrhage into the portion of the intestine proximal to the cecum. Many rats also showed areas of hemorrhagic congestion in the lungs and mucous secretions in the tracheobronchial tree. These findings are typical of the hemorrhagic shock syndrome in the rat. Control animals that survived showed comparable changes but to a much lesser degree. Chlorpromazine protected survivors uniformly showed no evident gross pathology. The liver, spleen, and lungs, except for a slight pallor, were essentially normal in appearance. The small intestine was quite pale and contained only clear blood-free fluid.

TABLE II.—EFFECT OF CHLORPROMAZINE IN HEMORRHAGIC STRESS IN GROUP II

	Controls	*Chlorpromazine*
No. of rats	14	14
Survivals, per cent	(6/14) 42.8	(12/14) 85.6
Blood output survivals	3.90	3.01
Blood output deaths	3.65	2.70
Blood take-up survivals	0.01	0.00
Blood take-up deaths	0.79	0.27

DISCUSSION

These studies confirm earlier observations in this laboratory that pretreatment with chlorpromazine has a favorable influence on the survival rate of rats exposed to hemorrhagic hypotension. In addition, the data indicate that up to a point this drug can protect animals subjected to various degrees of hemorrhagic hypotension with equal efficiency. It is possible that additional factors contributing to irreversibility are generated in more profound types of shock and tend to sustain the decompensatory aspects of shock through pathways not susceptible to the influence of chlorpromazine. The breakdown of bacterial barriers as suggested by Fine (4), for example, may be such an additional factor since our observations show that bloodstream invasion by bacteria is unaffected by chlorpromazine.

The action of chlorpromazine should be interpreted only in the terms of the present experimental conditions, namely pretreatment with this specific dose of the drug. Broader implications concerning the beneficial effects of this agent may eventually prove valid, but there are too few controlled observations to warrant this at present. The dose of 2.5 milligrams per 100 grams body weight, used in this study, does not produce hypotension, except to a transient degree no longer evident at the time of the initial bleeding. Chlorpromazine in this dose range has an adrenolytic effect, blocking the pressor response to (2.0γ) epinephrine and norepinephrine given intravenously. The specific pharmacodynamic effect(s) that results in protection against stress is yet to be identified. Chlorpromazine has a diversity of pharmacologic actions in addition to its well-established effects on the central nervous system as described by Courvoisier and may be operating at a cellular level in several areas of the body.

Some of the factors characterizing chlorpromazine protection are suggested by the present study. The small uptake of blood from the reservoir during the hypotensive episode is one such factor. According to Fine

TABLE III.—EFFECT OF CHLORPROMAZINE IN HEMORRHAGIC STRESS IN GROUP III

	Controls	*Chlorpromazine*
No. rats	12	12
Survivals, per cent	(4/12) 33.3	(11/12) 91.0
Blood output survivals	4.03	3.60
Blood output deaths	3.87	3.04
Blood take-up survivals	0.11	0.03
Blood take-up deaths	1.11	0.00

TABLE IV.—EFFECT OF CHLORPROMAZINE IN HEMORRHAGIC STRESS IN GROUP IV

	Controls	*Chlorpromazine*
No. of rats	14	9
Survivals, per cent	(8/14) 57.1	(8/9) 88.8
Blood output survivals	3.91	3.15
Blood output deaths	3.26	3.30
Blood take-up survivals	0.19	0.03
Blood take-up deaths	1.14	0.80

(3) Shorr (10), and others, the total volume of blood lost in a shock experiment is not as valid an index of the magnitude of the stress to which an animal is exposed as is the degree of vascular decompensation that develops from the hemorrhagic stress. A decompensatory tendency is mirrored by the need for blood take-up to an extent that the volume of self-infusion required is a measure of the degree of decompensation. When the decompensatory tendency is uncorrected, it inevitably, with time, leads to irreversibility. Absolute protection would be indicated by zero uptake values and, of course, by 100 per cent survival, both of which are a measure of optimal compensatory adjustment. The treated animals in the first four groups of rats approach these criteria much more closely than their controls. This is interpreted to indicate that chlorpromazine is effective in blunting, although not completely eliminating, the progressive decompensatory vascular tendency characteristic of the lethal shock syndrome.

In experimental shock the overall deterioration of the circulation is closely related to the sequestration of blood in the large splanchnic vascular beds. Whether this pooling of blood is an intrinsic cause of irreversibility or whether it is a consequence of some other fundamental shock syndrome lesion is quite unsettled. Chlorpromazine, in both hemorrhagic shock experiments and in tumbling shock experiments, was highly effective in this regard; rats subjected to ordinarily lethal bleeding procedures did not develop visceral congestive changes. This was in contrast to the fatal, unprotected cases, in which the typical congested and hemorrhagic bowel was uniformly demonstrated at autopsy.

The character of the respiration during the hypotensive period is also modified by chlorpromazine. Respiration in the untreated rats in shock is typically rapid, irregular in pattern, and even gasping with an exaggerated diaphragmatic component. In the treated animals the nature of the respiratory movements following hemorrhage is similar to that seen prior to bleeding. The rate is moderately faster, it remains regular, and the air-hunger type of gasping does not occur. The preservation of a more normal pattern of respiration during shock suggests that the beneficial action of chlorpromazine may involve a modification of the response of the central nervous system to stress.

These experiments with chlorpromazine in hemorrhagic shock tend further to delineate the properties of this agent. Chlorpromazine represents an important experimental tool to gain insight into the basic mechanisms of the shock syndrome by virtue of its effects on critical homeostatic systems. While the latter are not identified by this study, the data point to a number of stigmas of the protected state as generated by chlorpromazine. These stigmas, in addition to increased survival, are (1) the attenuation of gross circulatory decompensation in hemorrhagic shock with little need for blood infusions after several hours of drastic hypotension, (2) the elimination of sequestration of blood from

TABLE V.—EFFECT OF CHLORPROMAZINE IN HEMORRHAGIC STRESS IN GROUP V*

	Controls	*Chlorpromazine*
No. of rats	23	21
Survivals, per cent	(10/23) 43.4	(11/21) 52.4
Blood output survivals	4.19	3.91
Blood output deaths	3.99	3.72
Blood take-up survivals	0.97	0.13
Blood take-up deaths	0.93	0.49

*This group not considered protected by chlorpromazine.

the active circulation in the splanchnic vascular bed, and (3) the blunting of characteristic and exaggerated cardiorespiratory autonomic responses to severe stress.

SUMMARY

1. Rats pretreated with chlorpromazine and subjected to five grades of hemorrhagic hypotension showed a significantly increased survival rate when compared with untreated controls, except in animals subjected to the severest bleeding procedures.

2. The chlorpromazine treated survivors showed a minimal tendency to take up blood spontaneously from the reservoir during the period of hypotension.

3. Survivors in the drug treated group were found to be free of visceral congestion and hemorrhage consistently noted in untreated controls.

4. Chlorpromazine treated animals showed more favorable respiratory patterns and pulse rates during hemorrhagic hypotension.

REFERENCES

1. Baez, S., Zweifach, B. W., Pellon, R., and Shorr, E. A renal factor in vascular response to hemorrhagic and traumatic shock. Am. J. Physiol., 1951, 166: 658.
2. Baez, S., Zweifach, B. W., and Shorr, E. Protective action of dibenamine against the fatal outcome of hemorrhagic and traumatic shock in rats. Fed. Proc., Balt., 1952, 11: 7.
3. Courvoisier, S., Fournel, J., Ducrot, R., Kolsky, M., and Koetschel, P. Propriétés pharmacodynamiques de chlorhydrate de chloro-3-(demethylamine-3-propyl)-10-phenothiazine (4560 R. P.). Arch. internat. pharm. dyn., Par., 1953, 92: 305.
4. Fine, J. The Bacterial Factor in Traumatic Shock. Springfield, Ill.: Charles C Thomas, 1954.
5. Fine, J. and Seligman, A. M. Traumatic shock; an experimental study including evidence against the capillary leakage hypothesis. Ann. Surg., 1943, 118: 238.
6. Hershey, S. G., and Guccione, I. Protective action of chlorpromazine in hemorrhagic shock in rat. Fed. Proc., Balt., 1955, 14: 351.
7. Hershey, S. G., Zweifach, B. W., and Metz, D. B. An evaluation of the protective action of autonomic blocking agents in peripheral circulatory stress. Anesthesiology, 1954, 15: 589.
8. Laborit, H., and Huguenard, P. Artificial hibernation in cases of severe shock. Presse méd., 1953, 61: 1029.
9. Remington, J. W., Hamilton, W. F., Boyd, G. H., Hamilton, W. F., Jr., and Caddell, H. M. Role of vasoconstriction in response of dog to hemorrhage. Am. J. Physiol., 1950, 161: 116.
10. Shorr, E., Zweifach, B. W., Furchgott, R. F., and Baez, S. Hepatorenal factors in circulatory homeostasis—IV, tissue origins of vasotropic principles, VEM and VDM which appear during evolution of hemorrhagic and tourniquet shock. Circulation, 1951, 3: 42.

A STUDY OF 50,000 SPECIMENS OF THE HUMAN VERMIFORM APPENDIX

DONALD C. COLLINS, M.D., M.S.(Path. & Surg.), Sc.D., F.A.C.S., Hollywood, California

A CONTINUING STUDY on the human vermiform appendix has been in progress since 1924. During these past 32 years the records of certain hospitals in San Francisco, Rochester, Minnesota, the United States Army Medical Department—during World War II and finally in both Los Angeles and Hollywood, California, have been constantly tabulated and recorded whenever the appendix was removed. These appendectomies represent the combined skill of over 250 leading American surgeons. The pathologic diagnoses constitute the opinion of scores of highly trained and qualified American pathologists. The hospitals where the surgical and pathologic records were studied had approval by The American College of Surgeons and were representative of the finest types of modern American hospitals. From time to time during the span of the past 32 years, 22 contributions have been published in the American medical literature covering various interesting subjects in this continuing study. This presentation will conclude our long study upon this subject. It is hoped that some of the results obtained will be of both interest and value to other subsequent workers in this particular field of medicine.

It is readily admitted that in the earlier years, many interesting pathologic entities went unrecognized, and, as a consequence, the total incidence figures of specific pathologic conditions may, in all probability, be too low. This impression was recently partially substantiated (21, 22) when a review was made of older microscopic slides to determine the approximate incidence of Histoplasma capsulatum in the vermiform appendix. It was soon apparent that many instances had gone unrecognized in the earlier years of this study. Similarly, the examples of marked hyperplasia of both Meissner's and Auerbach's plexi and even large neurofibromas were not recorded by the hospital pathologist in the earlier years. It is gratifying after these many years finally to be able to record at present almost a thousand-fold decrease in the hospital mortality of instances of acute appendicitis.

TABLE I.—SOURCE OF MATERIAL

	No. of cases	*Per cent of 50,000*
Surgical	(45,335)	(90.67)
Acute		
1. Perforative or gangrenous	4,911	9.822
2. Simple acute	7,107	14.214
Subacute	6,819	13.638
Chronic	16,617	33.234
Prophylactic appendectomy	9,248	18.496
Miscellaneous lesions	633	1.266
Postmortem	(4,665)	(9.330)
Various (4, 134—82.68%—stated not remarkable)	4,665	9.330
Totals	50,000	100.00

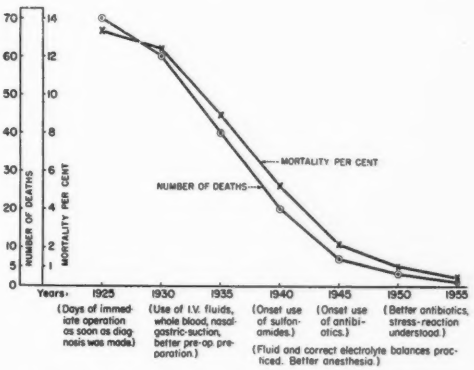


CHART 1. Composite mortality for all types of acute appendicitis.

From the Department of Surgery, College of Medical Evangelists, Los Angeles.

TABLE II.—SPECIFIC DISEASES

	No. of cases	*Per cent of 50,000*
Mesenteric lymphadenitis	902	1.804
Tuberculosis, secondary	141	0.282
Diabetes mellitus	125	0.250
Acute and chronic ulcerative colitis and enteritis	123	0.246
Syphilis, secondary	109	0.218
Pyelophlebitis and liver abscesses	61	0.122
Carcinoma of the cecum	59	0.118
Acute exanthem (measles: 28, scarlet fever: 2)	32	0.064
Bacillary dysentery	29	0.058
Traumatic blow to the anterior abdominal wall	28	0.056
Epidemic parotitis	20	0.040
Brucellosis	9	0.018
Tularemia	6	0.012
Tsutsugamushi's disease (scrub typhus)	6	0.012
Syphilis, gumma	5	0.010
Leptospirosis (Weil's disease)	5	0.010
Hodgkin's disease	4	0.008
Relapsing fever	4	0.008
Leprosy, secondary	3	0.006
Small pox	3	0.006
Epidemic hepatitis	3	0.006
Typhoid fever	3	0.006
Torulosis	2	0.004
Yellow fever, pellagra, and oroya fever (1 each)	3	0.006
Totals	1,685	3.370

TABLE III.—MYCOLOGIC PARASITIC DISEASES

	No. of cases	*Per cent of 50,000*
Histoplasmosis (H. capsulatum)	3,905	7.810
Amebiasis (all pathogenic species)	2,510	5.020
Giardiasis	61	0.122
Coccidioidomycosis	11	0.022
Algid malaria	7	0.014
Balantidial dysentery	6	0.012
South American blastomycosis, disseminated	3	0.006
Cryptococcosis	3	0.006
Sporotrichosis	2	0.004
Geotrichosis	1	0.002
Totals	6,509	13.018

TABLE IV.—PARASITIC WORMS

	No. of cases	*Per cent of 50,000*
Enterobius vermicularis	319	0.638
Trichinella spiralis	191	0.382
Trichuris trichiura	146	0.292
Ascaris lumbricoides	97	0.194
Necator americanus	51	0.102
Taenia ecchinococcus cysts, secondary	31	0.062
Taenia saginata	24	0.048
Strongyloides stercoralis	21	0.042
Hymenolepis nana	17	0.034
Taenia solium	16	0.032
Diphyllobothrium latum	11	0.022
Paragonimus westermani	9	0.018
Ancylostoma duodenale	7	0.014
Schistosoma mansoni	6	0.012
Schistosoma japonicum	5	0.010
Fasciolopsis buski	2	0.004
Wuchereria bancrofti	2	0.004
Fasciola hepatica	1	0.002
Totals	956	1.912

TABLE V.—MISCELLANEOUS PATHOLOGIC CONDITIONS

	No. of cases	*Per cent of 50,000*
Melanosis Mucosae Appendicis Vermiformis (4)	(7,119)	(14.238)
Severe	181	0.362
Mild	6,938	13.876
Hyperplasia of Auerbach's and Meissner's plexi (4, 6)	1,001	2.002
Diverticula (7)	(691)	(1.382)
Acquired, inflammatory type	684	1.368
True, congenital type	7	0.014
Benign lymphoma	363	0.726
Mucocele (myxoglobulosis: 8, calcification: 4)	112	0.224
Subserosal cysts (17)	95	0.190
Benign mucosal polyps (3)	36	0.072
Endometriosis (18)	27	0.054
Benign giant lymphoid hyperplasia	23	0.046
Benign mucosal polyps associated with congenital familial polyposis	17	0.034
Totals	9,484	18.968

TABLE VI.—BENIGN TUMORS

	No. of cases	*Per cent of 50,000*
Leiomyoma (including leiofibromyoma (4)	830	1.660
Neuroma (13)	591	1.182
Lipoma (4)	203	0.406
Neurofibroma	190	0.380
Fibroma	139	0.278
Ganglioneuroma (4)	126	0.252
Aberrant pancreas	37	0.074
Adenomyoma (4, 17)	28	0.056
Hemangioma	10	0.020
Myxoma	8	0.016
Lymphangioma	7	0.014
Hemangioendothelioma	1	0.002
Totals	2,170	4.340

TABLE VII.—PRIMARY MALIGNANT TUMORS

	No. of cases	*Per cent of 50,000*
Pseudomyxoma peritonaei (4,17) (From perforated appendiceal mucoceles)	270	0.540
Carcinoid tumors (4, 17, 20)	(261)	(0.522)
Localized to appendix	222	0.444
Metastasizing	39	0.078
Primary adenocarcinoma (4, 17, 20)	41	0.082
Reticuloendothelial sarcoma	11	0.022
Follicular lymphoblastoma	9	0.018
Lymphosarcoma	7	0.014
Malignant mucosal polyp, solitary (4, 17, 20)	6	0.012
Fibrosarcoma (17)	5	0.010
Undifferentiated sarcoma	(5)	0.010
Spindle-cell	2	
Round-cell	3	
Multiple myeloma	4	0.008
Melanoblastoma	3	0.006
Lymphangiosarcoma	2	0.004
Liposarcoma	2	0.004
Malignant mucosal polyp, associated with congenital familial polyposis	2	0.004
Neuroepithelioma	1	0.002
Neuroblastoma, myxosarcoma, and Boeck's sarcoid (1 each)	3	0.006
Totals	632	1.264

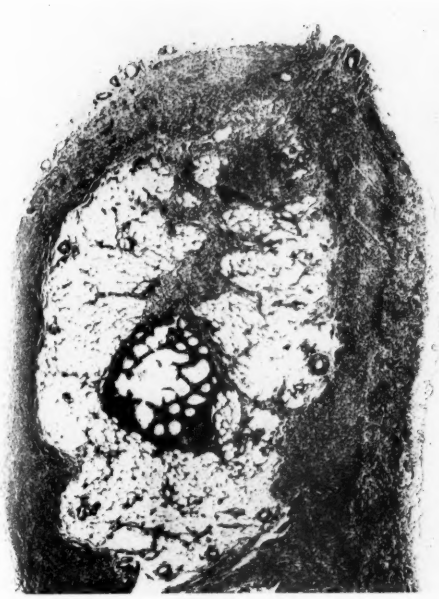


FIG. 1.

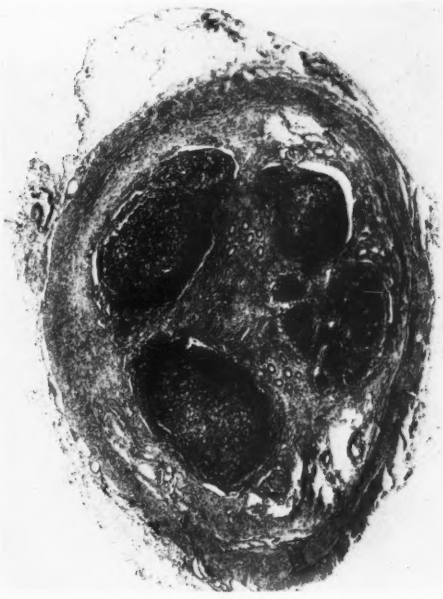


FIG. 2.

FIG. 1. Photomicrograph of tip of the appendix. This is a stage just prior to complete obliteration of the appendiceal lumen. A former severe acute inflammation produced this histologic picture. ×11.

FIG. 2. Photomicrograph of middle third of the appendix. This is an early example of very early complete obliteration of the appendiceal lumen. ×15.

This is a lasting monument to the marked improvements made in America and elsewhere of better preoperative and postoperative care of the appendectomized patient. This is especially true in the universal better understanding and management of the fundamental problems of normal human physiology, shock, stress, proper fluid and electrolyte balance, peritonitis, and the better employment of both bacteriostatic and bacteriocidal antibiotic agents.

The present study represents the combined "team-effort" of many American doctors and 11 leading hospitals during the past 32 years.

MATERIALS

In Table I are tabulated the source of the material for this report; 90.67 per cent were derived from surgically removed fresh specimens of the human vermiform appendix. The remaining 4,665 appendices (9.33 per cent) were obtained from postmortem material. Out of the total of 45,335 surgically removed specimens, 25,865 appendices (57.05

TABLE VIII.—FOREIGN BODIES IN THE LUMEN

	No. of cases	*Per cent of 50,000*
Fecoliths	(19,391)	(38.782)
Calcified	321	0.642
Noncalcified	19,070	38.140
Chronic barium retention	120	0.240
Lead shot	110	0.220
Wooden splinters and toothpicks	62	0.124
Various pieces of metal	60	0.120
Metal screw	51	0.102
Common metal pin	51	0.102
Nails	41	0.082
Fish bones	41	0.082
Animal bones (including chicken, etc.)	40	0.080
Needle	26	0.052
Plastic pieces	23	0.046
Metal safety-pin	7	0.014
Bubble-gum	3	0.006
Metallic mercury	3	0.006
Totals	20,029	40.058
less Fecoliths	−19,391	38.782
Unusual foreign bodies	638	1.276

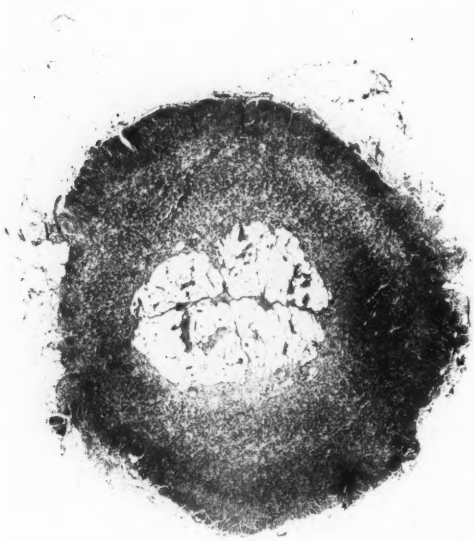


FIG. 3.

FIG. 4.

FIG. 3. Photomicrograph of middle third of the appendix. An example of very early complete obliteration of the lumen, the result of a recent acute inflammation. ×9.6.

FIG. 4. Photomicrograph of distal third of the appendix. Near the top of this illustration note that the blood vessels are thrombosed by masses of bacteria (Streptococcus pyogenes). There is a resultant acute infarction in the submucosa. Smaller vessels are thrombosed in the adjacent muscularis and subserosa. The blood supply of the appendix is of the terminal, end-artery type. ×11.

per cent) were diagnosed as being either "chronic" by the pathologist or prophylactically removed by the surgeon. Thus, more than half of all of these surgically removed specimens were essentially within the realm of normalcy; 12,018 examples were instances of acute appendicitis, of which 4,911 (10.83 per cent of the surgical appendices) were described as being either perforated or gangrenous; 13.64 per cent were diagnosed as representing "subacute appendicitis." An additional small group of 633 appendices (1.40 per cent) demonstrated miscellaneous significant pathologic lesions unrelated to inflammation or specific disease.

RESULTS

In Tables II through XII and in Chart 1 the essential data derived from this study are summarized. It is believed that these data are self-explanatory and require no further elaboration. Chart 1 graphically depicts the very laudable almost thousandfold decrease in hospital mortality for instances of acute appendicitis, from 13.9 per cent in 1925 to the present figure of 0.01 per cent in 1955. This chart should furnish all of the sermons necessary to convince others of the great strides made in American surgery during the past 30 years by private initiative and American "know-how," at least as far as appendicitis is concerned. The bibliography has been kept purposely limited in this final report. The previous 22 contributions upon the many phases of this subject have listed thousands of bibliographic references, under appropriate subdivisions. No useful purpose can be served by repeating that large amount of research data in this contribution. In passing, it is of great interest to note the very recent recognition of the common incidence of a very

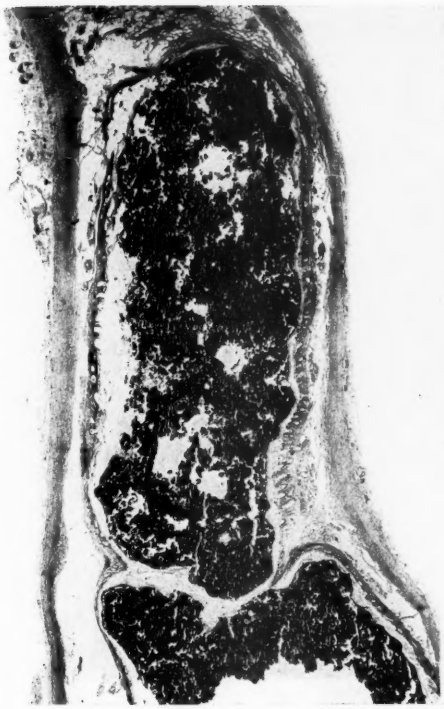


FIG. 5.

FIG. 6.

FIG. 5. Photomicrograph of middle third of the appendix. At the top of this illustration may be seen the junction line between an obliterated and a patent appendiceal lumen. More important still may be seen the rare "diaphragmatic occlusions" of Maale bridging the lumen at the base of this illustration. A single acute inflammation probably caused this histologic picture. ×8.5.

FIG. 6. Photomicrograph of middle third of the appendix. A rare subserosal cyst. ×9.8.

benign type of juvenile histoplasmosis. A recent review of our earlier microscopic slides of the vermiform appendix revealed that at least 7.81 per cent presented the characteristic Histoplasma capsulatum (Darling) in usually the "germinal-centers" of the submucosal lymph nodes.

CONCLUSIONS

1. A study of 50,000 specimens of the human vermiform appendix has been made, and results summarized for the continuous period from 1924 to May 1, 1955.

2. Ninety per cent of these appendices were surgically removed by more than 250 leading American surgeons, in 11 different approved hospitals.

3. The essential data derived from this long study have been condensed into 12 tables and 1 chart for the purposes of both clarity and brevity.

4. Happily, it can be reported that in this particular study there has been nearly a thousand-fold reduction in the hospital mortality for instances of acute appendicitis in the past 32 years. This fact testifies to the great progress made in America in the better preoperative and postoperative management of patients suffering from this disease of civilization.

5. Recently, it has been discovered on restudy, that at least 7.81 per cent of the specimens demonstrated the presence of the organism (yeast), Histoplasma capsulatum

TABLE IX.—APPENDICEAL FISTULAS

Type and location	*No. of cases*	*Per cent of 50,000*
External	(60)	(0.120)
Appendix joined to:		
1. Anterior abdominal skin. Supraumbilical—6 Infraumbilical—17	23	0.046
2. Lateral flank skin. Right side—36 Left side—1	37	0.074
Internal	(164)	(0.328)
Appendix joined to:		
1. Terminal ileum	46	0.092
2. Urinary bladder	31	0.062
3. Sigmoid colon	21	0.042
4. Cecum	20	0.040
5. Fallopian tube (Rt.—11, L.—2)	13	0.026
6. Right colon	12	0.024
7. Vagina	10	0.020
8. Rectum	3	0.006
9. Umbilicus	3	0.006
10. Right ureter	1	0.002
11. Duodenum	1	0.002
12. Gallbladder	1	0.002
13. Vena cava	1	0.002
14. Right common iliac vein	1	0.002
Totals	224	0.448

TABLE X.—OBLITERATION OF THE APPENDICEAL LUMEN

Degree of lumen obliteration	*No. of cases*	*Per cent of 6,710*
Total (4, 6, 11, 12, 13, 17, 20)	640	9.537
Two-thirds	701	10.446
One-third	1,012	15.080
(Appendices showing varying degrees of lumen obliteration)	(2,353)	(35.063)
None	4,357	64.920
Totals	6,710	99.983

Where stated in 6,710 specimens.

TABLE XI.—POSITION OF THE APPENDIX IN THE ABDOMINAL CAVITY

	No. of cases	*Per cent of 33,810*
Anterior to the cecum (1, 4, 5, 8)	(25,016)	(74.0090)
Caudad, toward the pelvis	10,017	29.6272
Mesiad, to cecum	12,702	37.5870
Laterad, to cecum	2,297	6.7948
Retrocecal (9, 10, 14, 15, 16, 20)	(8,794)	(26.0099)
Free	3,511	10.3844
Fixed in position	5,283	15.6255
Totals	33,810	100.0189

Where stated in 33,810 specimens.

(Darling). This finding indicates an unsuspected frequent incidence of a benign juvenile type of histoplasmosis here in America.

6. In 3.37 per cent of cases, specimens were removed during the course of various specific diseases and thus afforded a valuable means to learn what histologic changes occurred in the vermiform appendix.

TABLE XII.—MISCELLANEOUS RARITIES

Condition	*No. of cases*	*Per cent of 50,000*
Congenital agenesia (19)	4	0.008
True, congenital double appendix	2	0.004
Partial duplication or bifed appendix	2	0.004
Postinflammatory, pseudo-duplication (2)	1	0.002
Intussusception of appendix	2	0.004
Situs transversus viscerus abdominus	15	0.030
Associated with dextracardia—10		
Nonspecific periappendiceal and cecal granulomas	64	0.128
Abnormal position within the abdomen due to incomplete rotation of large bowel (4)	(2,003)	(4.006)
Appendix located in:		
L.L.Q. of abdomen	19	0.038
L.U.Q. of abdomen	27	0.054
R.U.Q. of abdomen	1,957	3.914
Meckel's diverticulum present	1,019	2.038
Pregnancy present	228	0.456
Fetal mortality: 77 died (33.77%)		
Maternal mortality: 21 died (7.21%)		
Appendix in hernial sacs	(977)	(1.954)
External	(525)	(1.050)
1. Indirect inguinal (sliding scrotal—171)	316	0.632
2. Ventral	92	0.184
3. Direct inguinal	74	0.148
4. Umbilical	34	0.068
5. Femoral	7	0.014
6. Obturator	2	0.004
Internal	(452)	(0.904)
1. Into various ileocecal fossae	423	0.846
2. Into paraduodenal hernial sacs	3	0.006
3. Into lesser omental sac	3	0.006
4. Into diaphragmatic hernial sacs	(23)	(0.046)
(a) Into left thorax	19	0.038
(b) Into right thorax	4	0.008

7. In 13.02 per cent of cases (including histoplasmosis), appendices demonstrated the presence of mycologic parasitic diseases.

8. Parasitic worms were found in 1.91 per cent of specimens.

9. Benign tumors were encountered in 4.34 per cent of these appendices.

10. Six hundred and thirty-two (1.26 per cent) primary malignant tumors were encountered.

11. Unusual foreign bodies were tabulated within the lumina of 1.28 per cent of specimens.

12. Only 224 instances (0.45 per cent) of appendiceal fistula were recorded.

FIG. 7.

FIG. 8.

FIG. 9.

FIG. 10.

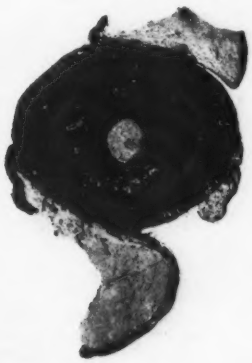


FIG. 11.

FIG. 7. Photomicrograph of distal third of the appendix. Note extensive endometriosis involving subserosa and muscularis. There is increased fibrosis. ×21.

FIG. 8. Photomicrograph of gross specimen. Appendix. Note the large balloon-shaped acquired diverticulum of the middle third. Two smaller diverticula can be seen on right side of this illustration at distal end of appendix.

FIG. 9. Photomicrograph of middle third of the appendix. Note the acquired inflammatory type of diverticulum extending from the lumen to the subserosal tissues. Such diverticula quickly perforate in the presence of acute inflammation. ×8.

FIG. 10. Photomicrograph of distal third of the appendix. The rare adenomyomas are depicted surrounding a diminished appendiceal lumen. ×6.

FIG. 11. Photomicrograph of distal third of the appendix. A benign neurofibroma fills the center of an obliterated appendix. ×6.5.

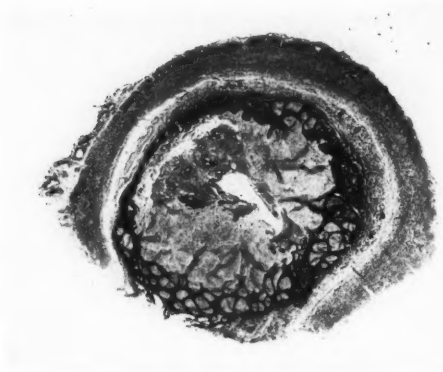


FIG. 12.

FIG. 13.

FIG. 14.

FIG. 15.

FIG. 12. Photomicrograph of proximal third of the appendix. Typical mucocele. Note that the lumen is distended and the mucosa demonstrates pseudocyst formation. ×8.

FIG. 13. Photograph of gross specimen. Appendix. Note a dark (orange) colored small tumor near the righthand side of this illustration at the tip of the appendix, adjacent to the ruler. This is a localized carcinoid tumor.

FIG. 14. Photomicrograph of middle third of the appendix. A primary adenocarcinoma fills the entire submucosa and is encroaching markedly upon the lumen. ×8.

FIG. 15. Photomicrograph of proximal third of the appendix. A primary fibrosarcoma has replaced nearly all the structures of this specimen and is markedly encroaching upon the lumen. ×11.

13. Among the interesting miscellaneous rarities found were: 4 examples of proved congenital agenesia, 2 instances of true congenital duplication, 2 cases of intussusception, and finally, 15 patients with situs transversus viscerum abdominis and 10 of these with a dextracardia.

14. In 6,710 appendices, it was stated that 9.54 per cent possessed total lumen obliteration; 25.52 per cent demonstrated varying

degrees of incomplete lumen obliteration; the remaining 64.92 per cent had completely patent lumina.

5. In 33,810 descriptions of the position occupied by the appendix within the abdominal cavity, 74 per cent were anterior to the cecum, while the remaining 26 per cent were stated to be retrocecal.

REFERENCES

1. Collins, Donald C. Historic phases of appendicitis. Ann. Surg., 1931, 94: 179–196.
2. Idem. Pseudoduplication of the vermiform appendix. Surg. Clin. N. America, 1931, 11: 921–926.
3. Idem. Adenomatous polyps of the vermiform appendix. Surg. Clin. N. America, 1932, 12: 1063–1067.
4. Idem. The chronic inflammatory and obliterative reactions of the vermiform appendix. Thesis. Post-Graduate School, University of Minnesota, June, 1932, 570 pp.
5. Idem. The length and position of the vermiform appendix; a study of 4,680 specimens. Ann. Surg., 1932, 96: 1044–1048.
6. Idem. The mechanism and significance of obliteration of the vermiform appendix. Thesis. Post-Graduate School, University of Minnesota, June, 1934, 92 pp.
7. Idem. Diverticula of the vermiform appendix. Ann. Surg., 1936, 104: 1001–1012.
8. Idem. Treatment of appendicitis. Am. J. Surg., 1937, 37: 440–445.
9. Idem. Hematuria associated with acute appendicitis. Urol. Cut. Rev., 1938, 42: 22–24.
10. Idem. Acute retrocecal appendicitis, based upon 751 instances. Arch. Surg., 1938, 36: 729–743.
11. Idem. Etiological factors in acute appendicitis. Surgery, 1939, 5: 267–270.
12. Idem. The present aspects of the appendicitis problem. J. Internat. Coll. Surgeons, 1941, 4: 325–330.
13. Idem. Present concepts in the management of both chronic and acute appendicitis. J. Internat. Coll. Surgeons, 1948, 11: 154–169.
14. Idem. The grave prognosis of appendicitis in the aged patient. Ann. West. M. & S., (May) 1948, 2: 193–205.
15. Idem. Excision of the appendix. Mod. Med., Chic., 1948, 16: 83.
16. Idem. Suppurative appendicitis. Mod. Med., Chic., 1949, 17: 82.
17. Idem. Unusual lesions of the vermiform appendix. Ann. West. M. & S., 1949, 3: 384–387.
18. Idem. Endometriosis of the vermiform appendix. Review of literature with addition of nine new instances, one of which caused severe melena. Arch. Surg., 1951, 63: 617–622.
19. Idem. Agenesis of the vermiform appendix. Am. J. Surg., 1951, 82: 689–696.
20. Idem. Unusual lesions of the vermiform appendix. Based upon a study of 24,326 specimens. Am. J. Proct., 1955, 6: 205-210.
21. Idem. Histoplasma capsulatum the principal cause of juvenile mesenteric lymphadenitis. Mississippi Valley M. J., in press.
22. Idem. The specificity of the "Starry Sky" phenomena in the submucosal appendiceal lymph nodes of juveniles with Histoplasma capsulatum infections. A preliminary report. Science, in press.

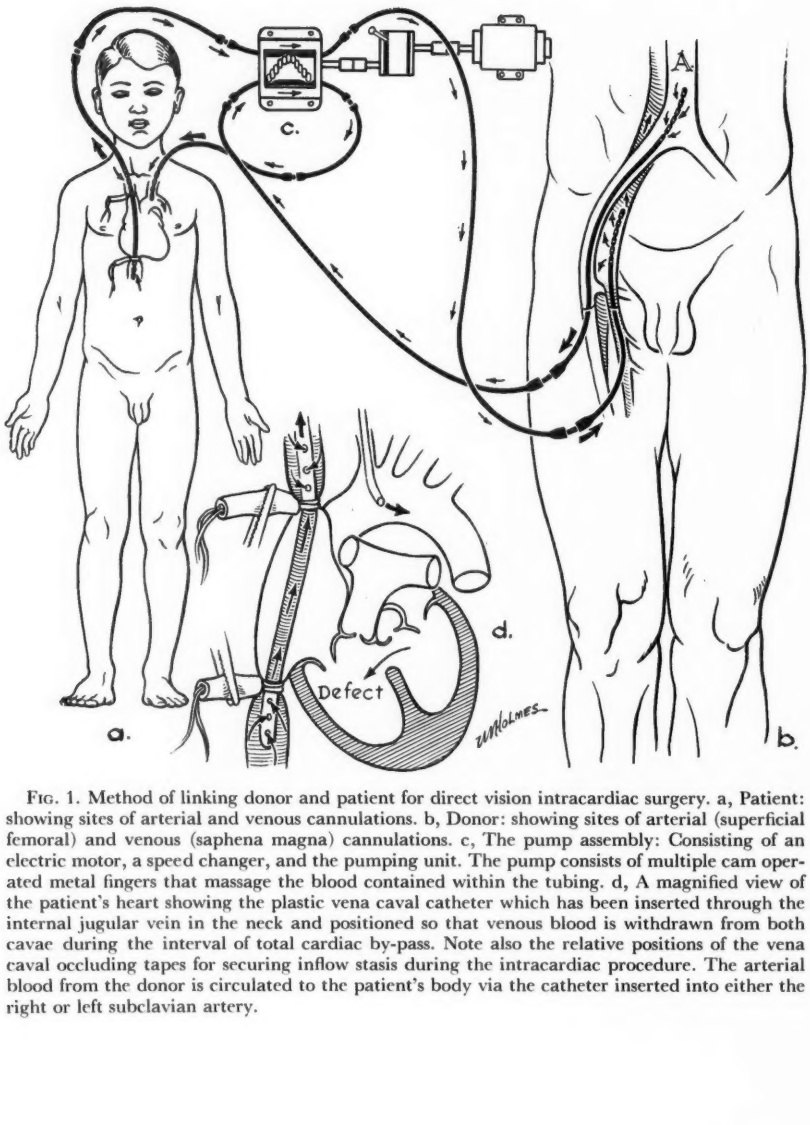


FIG. 1. Method of linking donor and patient for direct vision intracardiac surgery. a, Patient: showing sites of arterial and venous cannulations. b, Donor: showing sites of arterial (superficial femoral) and venous (saphena magna) cannulations. c, The pump assembly: Consisting of an electric motor, a speed changer, and the pumping unit. The pump consists of multiple cam operated metal fingers that massage the blood contained within the tubing. d, A magnified view of the patient's heart showing the plastic vena caval catheter which has been inserted through the internal jugular vein in the neck and positioned so that venous blood is withdrawn from both cavae during the interval of total cardiac by-pass. Note also the relative positions of the vena caval occluding tapes for securing inflow stasis during the intracardiac procedure. The arterial blood from the donor is circulated to the patient's body via the catheter inserted into either the right or left subclavian artery.

The Results of Direct Vision Closure of Ventricular Septal Defects in Eight Patients by Means of Controlled Cross Circulation.—C. Walton Lillehei, Morley Cohen, Herbert E. Warden, Newell R. Ziegler, and Richard L. Varco.

THE RESULTS OF DIRECT VISION CLOSURE OF VENTRICULAR SEPTAL DEFECTS IN EIGHT PATIENTS BY MEANS OF CONTROLLED CROSS CIRCULATION

C. WALTON LILLEHEI, M.D., F.A.C.S., MORLEY COHEN, M.D., HERBERT E. WARDEN, M.D., NEWELL R. ZIEGLER, M.D., and RICHARD L. VARCO, M.D., F.A.C.S.,

Minneapolis, Minnesota

THE IDEA OF CURING DISEASE by reciprocal blood transfer is as old as human history.[1] For many years experimentalists have utilized the reciprocal interchange of blood between donor and recipient animals as a valuable method for the elucidation of varied physiologic problems. Following Landsteiner's epochal contribution in 1900, clinicians also have found the technique useful for certain investigations. Still others have utilized, with impressive benefits, the reciprocal transfer of venous blood between the veins of donor and patient for therapeutic purposes in such conditions as uremia, toxemias of pregnancy, and erythroblastosis.

Historically, the first recorded observation that we have encountered, suggesting that cross circulation might be useful as a means of achieving total cardiac by-pass for intracardiac surgery was the report of Blum and Megibow in 1950. Their study was brief involving only 4 pairs of animals, but significant in that they utilized 2 of the elements that we have deemed essential for success, namely a pump to control the reciprocal interchange of blood, and perfusion of the animals at a much reduced rate of blood flow for the duration of the total by-pass period.

Kerr in 1951, Southworth and Pierce in 1952, and Glenn and Sewell in 1953 all successively utilized cross circulation experimentally for partial or complete cardiac by-pass, but their studies are less important due to their many technical difficulties doubtless engendered by their failure to use a pump to control the interchange of blood between donor and recipient animals. They also attempted to shunt much more blood than is necessary.

Andreasen and Watson in 1953 presented a detailed physiologic analysis of their important experiments utilizing cross circulation as a method for cardiac by-pass. They emphasized the value of a pump to control the interchange between donor and recipient. Likewise, they appreciated the full significance of the reduced flow concept based upon their earlier azygos flow studies (1). In their experiments they experienced difficulty in achieving an adequate venous return from the recipient dog and they incorrectly concluded that this occurrence represented an inherent limitation of the method which was due to venous capillary pooling in the recipient.

During this period experimental studies were being made in our laboratory upon the

From the Department of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota.

Dr. Morley Cohen is a Life Insurance Medical Research Fellow and Dr. Herbert E. Warden is a Trainee, National Heart Institute, United States Public Health Service.

Supported by Research Grants from the Graduate School, University of Minnesota, Minnesota Heart Association, Life Insurance Medical Research Fund, National Heart Institute, United States Public Health Service (H-830), and the Minnesota Cardiovascular Fund.

[1]Ovid's *Metamorphoses* relates how the witch, Medea, rejuvenated Jason's aged father, Aeson, by slitting his throat to let out his ancient blood replacing it with a concoction of herbs and offal of birds and animals so that body and mind returned to their state of 40 years before.

physiology of total cardiac by-pass (4) at reduced rates of flow (6, 7) and upon the creation and closure of atrial or ventricular septal defects utilizing either an autogenous lung (5) or controlled cross circulation (15) as the method of purifying the blood. These experimentally developed techniques have culminated in the successful closure of ventricular septal defects in man (7, 15) by open cardiotomy utilizing total by-pass of the heart and lungs achieved by means of controlled cross circulation. These reports which were published in 1954 mentioned the preliminary results obtained in the 8 patients herein reported.

APPLICATION IN MAN

This present report describes the techniques utilized and provides additional information concerning these first 8 patients to have ventricular septal defects closed. Moreover, 4 of these 8 patients have now had cardiac recatheterization studies performed postoperatively. This technique for direct vision intracardiac surgery also has made possible the performance of corrective surgery for other intracardiac defects (12) such as tetralogy of Fallot and atrioventricularis communis heretofore classed either as not operable or as subjects for palliative surgery only.

The cross circulation method utilizes the simultaneous reciprocal exchange of equal quantities of compatible arterial and venous blood between the patient and a normal donor. A pump is utilized to control accurately this interchange of blood between patient and donor. Under these conditions with the circulatory systems of the patient and donor suitably linked together, the patient's cardiac venous inflow may be totally occluded, a cardiotomy performed, and an intracardiac procedure carried out under direct vision with adequate time at the surgeon's disposal.

All of these patients have been operated upon at normal body temperature to obviate the deleterious effects of reduced body temperature upon the ventricular conduction mechanism. The azygos flow experimental studies (1, 4–7, 14, 15) have demonstrated conclusively the advantages as well as safety of total by-pass of the heart and lungs carried out at normal body temperatures with perfusion of the circulatory system at rates of blood flow substantially below the basal or resting cardiac output.

METHOD IN MAN

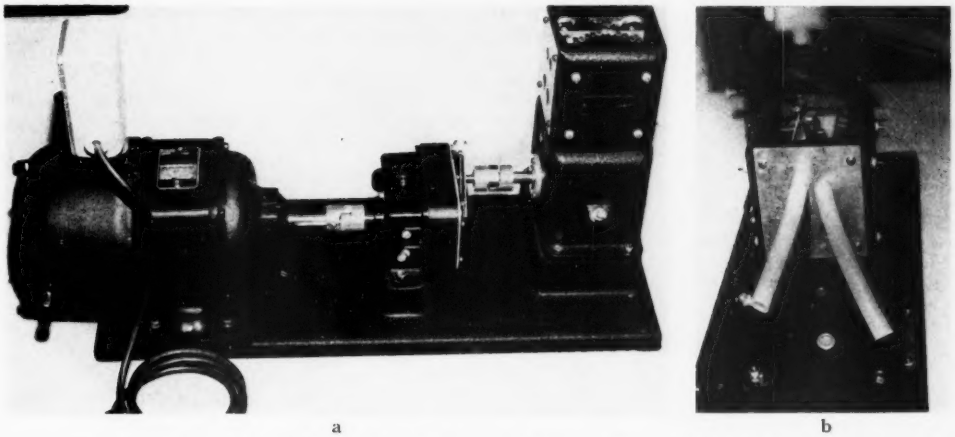
Figure 1 illustrates diagrammatically the method of linking together the circulatory systems of the patient and donor for the reciprocal exchange of arterial and venous blood permitting the heart and lungs of the patient to be totally by-passed for sufficient intervals to allow definitive surgery under direct vision.

For this operative procedure the patient has been placed in a supine position upon the operating table, and the heart and great vessels have been exposed by entering the chest through an anterior bilateral thoracotomy in the third or fourth interspace transecting the sternum transversely. After incising the pericardium the caval entrances at the auricle are dissected from the adjacent tissues cardiac to the azygos and hepatic veins respectively. Tapes are then passed around these veins as indicated in Figure 1.

Cannulations in the patient.[2] The patient's vena caval cannula has been inserted via the right or left jugular vein after exposing it in the neck through a short supraclavicular incision.[3] The openings at the tip of this caval catheter were positioned in the inferior vena cava below the lower occluding tape and the accessory holes cut higher along the shaft of the catheter were placed in the superior vena cava cephalad to the upper occluding tape. Thus, during the cardiac by-pass interval this catheter effectively drained venous blood returning to both of these caval systems.

[2]The catheters utilized to cannulate these vessels in the patients and the donors were standard commercially manufactured thin walled plastic nasal oxygen catheters 12 f to 14 f in size. The 12 f size was utilized in the infants and the 14 f size was found suitable for the older children.

[3]Currently, we prefer cannulation of the cavae by the transauricular insertion of individual catheters connected by a *y* adaptor.



a b

FIG. 2. The pumping assembly for controlled cross circulation. a, This pump controls the reciprocal exchange of blood between the patient and donor. Note the explosion proof electric motor (¼ h.p.) on the left, speed changer transmission in the center, and the pump unit consisting of multiple cam operated metal fingers which impart a unidirectional movement to the blood contained within flexible tubing by external massage. There are only two controls; the regulator for the speed changer, and a switch for the motor. b, Close-up of the endplates designed to hold the 2 extracorporeal circuits at the same level within the pumping unit for ease in calibration of the flow.

The predetermined volume of arterial blood from the donor was circulated to the patient's arterial system via a catheter inserted into the right[4] subclavian artery cannulated from within the chest. The tip of this catheter was positioned to lie in the ascending aorta (Fig. 1). In performing this cannulation the right subclavian artery was mobilized by ligating and transecting its branches (vertebral, internal mammary, costocervical, and thyrocervical trunk) in a manner similar to that generally employed preparatory to performing a subclavian-pulmonary artery anastomosis for tetralogy of Fallot. The next step was to divide the subclavian artery between ligatures at the apex of the chest, and then its proximal end was threaded out from behind the right vagus nerve (with care to preserve the recurrent laryngeal nerve). This maneuver greatly facilitated the subsequent introduction of the catheter tip, after application of a Potts type occluding clamp to the proximal subclavian artery, to a position in the ascending aorta.

[4]The left subclavian artery has been found to be equally satisfactory.

Donor cannulations.[5] The donor cannulations have been performed through a short incision 2 fingerbreadths below either the right or left inguinal ligament exposing the great saphenous vein and the superficial femoral artery. The donor's venous catheter has been threaded into the saphenous vein so that its tip lies in the iliac vein or inferior vena cava. The donor's arterial catheter has been inserted into the superficial femoral artery through a small incision and is positioned so that its multiple-holed tip lies within the abdominal aorta. This latter maneuver is vital to assuring an adequate supply of blood at all times and has eliminated the possibility of the vessel wall collapsing about the catheter and thus obstructing it during the perfusion (as might be possible were this catheter within a smaller branch of the aorta).

Anticoagulants. Just prior to the insertion of these catheters both the donor and the patient were each given a single intravenous dose of heparin (0.75 mgm./lb. body weight).

[5]The catheters utilized to cannulate these vessels in the donors were standard commercially manufactured thin walled plastic nasal oxygen catheters 12 f to 14 f in size.

TABLE I.—DIRECT VISION SUTURE REPAIR OF INTERVENTRICULAR SEPTAL DEFECTS BY MEANS OF CONTROLLED CROSS CIRCULATION

Patient	Sex	Age, yrs.	Wt., kgm.	Duration (min. & sec.) Total occlusion of venae cavae	Pump on	Flow rate c.c./min. Total	Per kgm.	Plasma hgb.,* mgms. per cent	Patient outcome	Donors Relationship Age, yrs.	Complications
Case 1, G.G.	M	1	6.9	13′02″	18′56″	280	40	2	Died 11 days postop. of pneumonia and tracheobronchitis	Father 39	None
Case 2, B.M.	M	4	16	26′35″	27′30″	600	37	12	Successful closure	Father 26	None
Case 3, P.S.	F	5	14.5	10′30″	13′29″	590	40	10	Successful closure	Father 26	None
Case 4, L.T.	F	9½ mos.	9.3	8′13″	9′00″	375	40	2	Successful closure	Father 31	None
Case 5, T.F.	M	1	7.2	9′00″	12′00″	300	40	5	Died 4 days postop. of atelectasis of only functional lung	Mother 29	None
Case 6, C.L.	F	1	5.2	7′00″	9′39″	196	37	7	Successful closure	Great Uncle 54	None
Case 7, K.H.	F	5	11.4	12′07″	12′26″	400	34	30	Successful closure	Father 37	None
Case 8, M.G.	F	5 mos.	5.5	5′10″	13′33″	220	40	17	Successful closure	Mother 32	None

*Blood drawn from donor's antecubital vein within 30 minutes of conclusion of perfusion.

Following conclusion of the intracardiac procedure the patient usually has been given a similar quantity of protamine sulfate (0.75 mgm./lb. body weight), although in several patients the use of protamine has been omitted with no detectable ill effects. No protamine has been given to any of the donors. These relatively small doses of heparin suffice in this set-up because of the limited surface area of the extracorporeal contacts for the blood. In addition, abnormal postoperative hemorrhage has not been a problem quite likely because platelets and fibrinogen are not removed from the blood in this system by contact with relatively large areas of foreign surface.

Pump. The pump functions to control accurately the reciprocal exchange of blood and thus prevents any serious quantitative disproportion. The pump model utilized in this clinical operation is unchanged from that used in the previously reported experimental and clinical studies (5-7, 14, 15) (Fig. 2).

The pumping action is exerted by external pressure applied through multiple cam operated metal fingers which massage the blood contained in the extracorporeal tubing in a unidirectional flow. This type pump has been found to be simple to operate, reliable, relatively inexpensive, and readily obtainable since this pumping principle has been used commercially for a variety of tasks. The only adaptation that we have found advisable to make in the commercially supplied pump was to design a pair of metal end plates to hold the tubing of each of the two circuits at the same level within the pump (Fig. 2b). This alteration makes it easier to adjust the outputs of these two circuits so that they remain equal. The entire system has only two controls: the variable speed changer transmission which is set ahead of time by direct calibration (with water) to deliver the rate of flow desired and the power switch to turn the electric motor on and off. The pump mechanism does not contact the blood directly and thus needs no sterilization. The plastic tubing[6] and catheters making up the extracorporeal circuits have been sterilized by soaking in aqueous zephiran chloride 1 to 1,000 for 48 hours. The short lengths of gum rubber tubing between the cam operated fingers were heat sterilized. This plastic and rubber tub-

[6]This plastic tubing is now heat sterilized also.

TABLE II.—PREOPERATIVE CARDIAC CATHETERIZATION DATA FOR PATIENTS WITH VENTRICULAR SEPTAL DEFECTS

Patient	Age at cath.	Pressure (mm. Hg) R.A.	R.V.	P.A.	Systemic artery	Oxygen saturation, per cent* Sup. cava	Inf. cava	R.A.	R.V.	P.A.	Systemic artery
Case 1, G.G.	7 mos.	.....	48/10	46/40	65/45	..	71	68	85	..	94
Case 2, B.M.	22 mos.†	.....	30/0	30/11	.....	71	..	70	83	82	95
Case 5, T.F.	1 yr.	15/4	55/0	55/20	60/50	56	50	52	77	73	92
Case 8, M.G.	5 mos.	.....	70/−4	60/30	75/60	..	51	50	85	81	95

*All determinations made by Van Slyke method of analysis.
†Closure of ventricular septal defect not undertaken until 2 years later at age 4 years.

TABLE III.—CARDIAC CATHETERIZATION DATA BEFORE AND AFTER CLOSURE OF VENTRICULAR SEPTAL DEFECTS

Patient	Age at cath.	Time relationship of cath. to surgery	Pressure (mm. Hg) R.A.	R.V.	P.A.	Systemic artery	Oxygen saturation, per cent* Sup. cava	Inf. cava	R.A.	R.V.	P.A.	Systemic artery
Case 3, P.S.	14 mos.	4 yrs. before	...	65/0	60/40	85/60	..	74	52	80	85	..
		4 mo. after	8/0	60/0	60/28	.....	76	..	70	67	68	94
Case 4, L.T.	9 mos.	1 mo. before	8/4	64/0	60/20	.....	66	..	66	86	85	98
		5 mo. after	...	40/0	.....	.....	..	48	66	65	..	..
Case 6, C.L.	10 mos.	2 mo. before	1/0	54/−6	42/11	.....	30	..	32	87	90	96
		6 mo. after	...	25/0	20/8	68/50	..	65	69	71	66	95
Case 7, K.H.†	5 yrs.	1 mo. before	...	80/15	80/66	70/54	70	71	75	90	89	96
		9 mo. after	...	29/2	29/9	.....	69	..	73	72	72	94

*All determinations made by Van Slyke method.
†Had multiple (three) ventricular defects closed at surgery.

ing is disposed of after each perfusion and thus poses no problems in resterilization.

Body temperature. All of these patients were operated upon at normal body temperature because our previous observations in the experimental laboratory have indicated to us that reductions in body temperature are frequently associated with serious and often fatal cardiac conduction difficulties (ventricular fibrillation, complete heart block) when surgical procedures are performed within the ventricles. At normal temperature the myocardium has a significantly greater resistance to these complications.

Quantity of blood perfused. The preselected flow for each operation has been determined on the basis of the patient's body weight and the data derived from the aforementioned azygos flow experimental studies (6, 7). These experimental studies indicated to us that during intervals of total cardiac by-pass attempts to circulate the full amount of the so-called resting or basal cardiac output were completely unnecessary and actually detrimental for several reasons of which may be mentioned the increased complexities and thus dangers of the techniques required to pump larger quantities of blood as well as the fact that coronary sinus and thebesian blood loss during open cardiotomy was significantly increased thereby.

In these 8 clinical operations the pump was calibrated to deliver arterial blood from the donor at a rate of 34 to 40 cubic centimeters per kilogram of patient body weight per minute and to remove an equal quantity from the patient's cavae for return to the donor during the interval of the total cardiac by-pass (Table I). This quantity of blood probably represents about 30 per cent of the normal cardiac output at rest for children of this size. The optimum quantity to circulate during total by-pass has not been precisely determined as yet, but there has been no evidence whatsoever in these first 8 patients of any deleterious sequelae attributable to these lowered flow rates.

Blood loss replacement. The donor does not experience any net loss of blood during the perfusion since the pump is set to return to him the same amount of venous blood as leaves via his arterial catheter. The patient's

blood losses from the operative wound and from that aspirated from the interior of the heart during cardiotomy were replaced intravenously by means of a cannula in the saphenous vein through which citrated blood was introduced in the usual manner. In none of these patients has the coronary sinus blood aspirated from the interior of the heart been returned to the patient's or donor's circulation because of the trauma (hemolysis) imposed upon this blood by an effective aspirator. Careful weighing of all patients in the operating room immediately preoperatively and postoperatively has been found to be a rapid, simple, and accurate index of their blood volume.

SELECTION OF PATIENTS FOR OPERATION

All of the 8 patients selected for surgical correction have been symptomatic, most rather severely so, and with pulmonary hypertension. All 8 have represented patients who were judged by our cardiologists as unlikely to survive for more than a short interval without surgical correction. In fact 4 of these patients (G.G., T.F., C.L., and M.G., Table I) were unable to exist outside of a hospital at the time of their surgery, and each of the other 4 patients had spent frequent and long periods in hospitals because of their disability.

The principle symptoms observed in these patients consisted of various combinations of growth failure, dyspnea, reduced exercise tolerance, cardiac decompensation, and repeated episodes of pneumonia. All of these patients had cardiomegaly.

All 8 patients have had preoperative cardiac catheterization, and in 7 the pulmonary hypertension was severe averaging more than 75 per cent of their measured systemic (arterial) blood pressure. In the 1 case in which the pulmonary pressures were only modestly increased (B.M., Table II) the cardiac catheterization study had been done 2 years prior to surgery. None of these patients was clinically cyanotic at rest; but several had a history of cyanosis when crying, exercising, or with their episodes of pneumonia. Additional details concerning the preoperative status of these patients are supplied in the case reports and in the summary Tables II and III.

SELECTION OF DONORS

None of the patients or donors undergoing the cross circulation procedure has exhibited any evidence of blood incompatibility reactions. Thus, despite our limited experience to date, the complete freedom from this complication may warrant an expression of the principles involved.

Good physical health is required together with freedom from a history of syphilis or a past history of hepatitis or malaria within 5 years. The other usual criteria applicable to routine blood donors are observed. In addition, we have customarily performed a chest roentgenogram, electrocardiogram, complete blood count, and urinalysis on all prospective donors to detect any evidences of serious abnormalities. More specifically, the following four general principles are believed to be of value in regard to the blood typing and cross matching:

1. The blood of donor and patient must be homologous with respect to the ABO system. Donors who have not had previous transfusions are preferred because of the increased hazards of possible sensitizations from prior transfusions.

2. The better known blood cell types have been determined (Table IV) and we believe it desirable that they be identical in donor and patient as well as in the other blood to be used for transfusion replacement to avoid potential immunizations. The number of such types that have been determined has to a certain extent depended upon the availability of specific antiserums.

3. If the blood cell types are not identical in the donor and the patient, then potentially serious immunizations should be avoided for both donor and patient, but particularly the healthy donor deserves this protection against future hazards should further blood transfusions become necessary at a later date. Likewise, in the case of donor

TABLE IV.—RELATIONSHIP OF BLOOD CELL ANTIGENS OF PATIENTS AND DONORS

			RH—hr											
	A	*B*	*C* *rh′*	*D* *Rho*	*Du*	*E* *rh″*	*c* *hr′*	*e* *hr″*	*M*	*N*	*Kell* *K*	*Cellano* *k*	*Duffy* *Fy*[a]	*Known Possible immunizations*
Case 1, patient G.G.	−	−	+	+		−	−	+	+	+	+	+	+	
M Father	−	−	+	+		−	−	+	+	+	+	+	+	None
Case 2, patient B.M.	+	−	+	+		−	+	+	−	+	−	+	−	Patient to Duffy a, M
M Father	+	−	+	+		−	+	+	+	+	−	+	+	
Case 3, patient P.S.	−	−	+	+		+	+	+	+	−	+	+	−	Father to C[s]
F Father	−	−	−	+		+	+	+	+	−	+	+	−	
(Mother)†	−	−	+	+		−	−	+	+	−	−	(+)	−	
Case 4, patient L.T.	+	−	+	+		+	+	+	−	+	−	+	−	Patient to M
F Father	+	−	+	+		−	+	+	+	+	−	+	−	Father to E
Case 5, patient T.F.	−	−	−	−		−	+	+	+	+	+	+	−	Patient to C, D
M Mother	−	−	+	+		−	+	+	+	−	+	−	−	Mother to Cellano, N
Case 6, patient C.L.	−	+	−	−	−	−	+	+	+	−	−	(+)	+	Donor to Duffy a
F Great Uncle	−	+	−	−	−	−	+	+	+	−	−	(+)	−	
Case 7, patient K.H.	+	−	−	−	−	−	+	+	+	+	−	(+)	+	Patient to D, E
F Father	+	−	−	+		+	+	+	+	+	−	(+)	+	
Case 8, patient M.G.	+	−	+	+		−	−	+	+	−	−	(+)	+	Patient to c
F Mother	+	−	+	+		−	+	+	+	−	−	(+)	+	

+Denotes the presence, and—the absence of the antigen tested for.
()indicates that the antigen was not tested for but inferred from the absence of its allelomorph.
*The presence of anti-C detected in the father's blood at 4 weeks, but not at 1 week.
†Mother not used as the donor, her cell types are listed as an illustrative example (see text).

women in the child bearing age, future pregnancies might provoke reactions should serious immunizations be permitted.

4. In the case of potentially less serious sensitizations, we prefer to have the patient rather than the donor accept the disadvantages of such possible immunizations.

When a suitable donor has been tentatively selected in accordance with these criteria, a saline centrifugal tube cross match and an indirect Coomb's test are performed as follows:

Two volumes of the patient's serum and also the donor's are added to 1 volume of once washed cells from the donor and patient respectively. Similarly, the serum of the patient and donor and cells from each additional bottle of bank blood intended for the patient's loss replacement during the surgical operation are tested for compatibility by the indirect Coomb's test. The serum of each bottle of bank blood is also tested with a saline suspension of cells of both patient and donor. These tests are carried out with occasional gentle shaking during incubation in a water bath at 37 degrees C. for 1 hour. All tubes are then centrifuged at 1,000 revolutions per minute for 1 minute. Those tubes containing donor's serum and patient's cells are next examined carefully for signs of hemolysis or agglutination. After gently resuspending the sediment, these observations are made over a concave mirror. Tubes containing the patient's serum and donor's cells are similarly examined after resuspension. These saline suspensions are then washed preferably 4 times and are used for the indirect Coomb's test. In this test, incubation proceeds for 15 minutes at room temperature after the addition of the antihuman serum. The material is then centrifuged at 500 revolutions per minute for 1 minute, the sediment carefully examined and resuspended by gentle shaking over a concave microscope mirror. If no agglutination is observed the sediment is examined on a slide microscopically for small clumps. Any degree of agglutination indicated incompatibility.

In Table IV we have outlined in detail the relationship of the blood cell antigens of patients and donors in these first 8 operations. These data serve to illustrate the application of the principles outlined. In this regard certain considerations are worthy of mention.

In Patient 1 (G.G.) it was possible to avoid sensitization of both donor and patient to all of the blood antigens for which tests were done.

In several of the cases (2, 4, and 5) there were differences in the MN cell types between the patient and donor; however, these types are known to be poor antigens, and thus the possibility of immunization occurring is slight.

In Patient 3 (P. S.) if the mother (cell types listed in Table IV) had been utilized as the donor, she would have been sensi-

tized to E (rh″), c (hr′), and Kell antigens by her daughter's blood. Each of these antigens has been implicated in erythroblastosis and hemolytic transfusion reactions. Since the father in this case was homozygous with respect to c (hr′), all of the children of these parents would carry the c (hr′) antigen, and the possibility of their having erythroblastosis fetalis would be high. The father on the other hand, who was utilized as the donor in this case, has been sensitized only to the C (rh′) antigen. However, this anti-C immunization can be readily detected by the cross matching procedures in common use. If he needs a transfusion at a future time, it would only be necessary to use Rh negative or C (rh′) negative Rh positive blood to avoid a possible transfusion reaction.

It should be emphasized at this point that these problems are in no way peculiar to the cross circulation technique, but apply equally well to all blood transfusions. It is a common observation that even today many blood banks or laboratories by incompletely typing all bank blood given for transfusions are sensitizing patients and thereby creating potentially serious transfusion problems for the future.

The indirect Coomb's test is done as a part of the cross match not only for cross circulation procedures, but routinely for all transfusions in this hospital. No cross circulation procedure should be undertaken without the benefit of this more sensitive technique.

Although some might question the need for such careful attention to the possibilities of immunization, we believe, that inasmuch as these operations are curative in scope rather than palliative, one is obligated to consider the patient's welfare beyond the immediate problem at hand.

We have recognized the desirability of testing for the S and Kidd antigens also, but sufficient amounts of these type specific antiserums have not been available to us to date. These antigens, like Kell and Duffy, are of importance because of their occasional participation in erythroblastosis and/or transfusion reactions and such sensitization is usually detectable only by an indirect Coomb's test.

In those cases as indicated in Table IV in which the blood cell types were not precisely identical, a unique opportunity has been provided to determine the development of antibody following the introduction of a single large dose of one or more antigens. Such follow-up studies are being made.

ANESTHESIA

In these cross circulation procedures both the donor and the patient are anesthetized. As a rule various combinations of nitrous oxide or cyclopropane have been employed for the patient's induction and then a change-over made to pentothal curare for the maintenance. The donors have usually received intravenous pentothal curare as their anesthetic agent.

During the actual by-pass interval the donors have been hyperventilated with 100 per cent oxygen. The value of increasing the donors respiratory minute volume by hyperventilation with oxygen in order to maintain a near normal *p*H in both the donor's and patient's blood during the by-pass interval has been established in our previous experimental studies (14). By maintaining the donor's alveolar carbon dioxide tension well below the normal range the effects of the metabolic acidosis which regularly develops during the total by-pass interval are counteracted. The patient's lungs during the total by-pass interval are not ventilated and are allowed to collapse out of the surgeon's way.

Both donor and patient are kept in a relatively light plane of general anesthesia at all times. The difference in size and body weight that has existed between the adult donors and many of these patients has not created any special anesthetic problems inasmuch as the depth of anesthesia is regulated by the blood concentration of the circulating agent and is independent of the body size.

THE INTRACARDIAC OPERATION

Following completion of the patient and donor cannulations as described; the pump, which has been set prior to the operation to give the approximate desired flow, is given a final check on its calibration at the operating table using sterile 5 per cent dextrose in distilled water. This procedure also serves to complete the irrigation of the plastic and rubber tubing making up the two extracorporeal circuits. When the flow in the two circuits is equal and calibrated at the desired rate, the donor and patient are linked together as indicated in Figure 1 so that the patient's aortic catheter receives the arterial blood from the donor's femoral artery cannula, and an equal quantity of venous blood is returned from the patient's caval system to the donor's venous catheter.

By leaving the extracorporeal tubing[7] filled with sterile isotonic dextrose solution no blood is needed to prime the system and the presence of any residual air bubbles is easily detected by visual inspection.

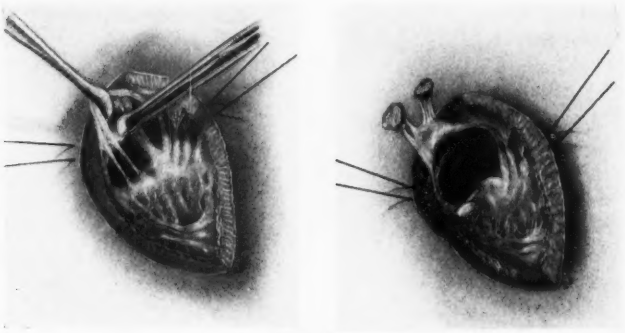
The pump is then turned on and the flow observed for a minute or two to verify the fact that the cross circulation is proceeding smoothly. Next, the patient's cardiac inflow is completely occluded by the tapes previously placed around the superior and inferior venae cavae. It is convenient for retraction purposes to insert two stay sutures which grasp widely and deeply the hypertrophied myocardium of the right ventricle. The right ventricle is then opened over most of its anterior surface by an incision paralleling the major branches of the coronary arteries (Fig. 3[8]).

Although differing considerably in their anatomic features, the ventricular defects in these 8 patients have uniformly occupied a characteristic position high in the ventricular septum, underneath the septal leaflet of the tricuspid valve (and partially hidden by the latter) and in juxtaposition to both the aortic leaflet of the mitral valve and to the cusps of the aortic valve. This is the area where the membranous portion of the ventricular septum should be. Viewed through a right ventricular cardiotomy in vivo the margins of these abnormal communications are only partly seen. They lie in the concealment of the septal cusp of the tricuspid valve and are fully visualized only after retraction on this leaflet (Fig. 4). Then, the inferior or lower margin of the defect is noted to consist of a definite muscular edge, which is the upper edge of the ventricular septum. Frequently the chordae tendineae of the septal cusp and of the anterior cusp of the tricuspid valve insert onto this inferior or (muscular) margin of the defect and occasionally they may even traverse the defect and insert into the septum on its left ventricular wall. This definite muscular

FIG. 3. Appearance of the ventricular septal defect from the right ventricle exposed by a surgical cardiotomy. Note the usual high location of the defect in the area of the membranous septum. The defect is characteristically partly concealed by the tricuspid valve leaflets, chordae tendineae, and to a variable extent by the papillary muscles.

[7]The extracorporeal circuits consist of plastic tubing (polyvinyl) with an internal diameter of 3/16 or ¼ inch and a wall thickness of 1/16 inch. Within the pump unit similarly or larger sized gum rubber tubing has been utilized instead of plastic because the greater elasticity of the former provides superior output from the pump.

[8]Figures 3 through 8 were drawn by our medical artist, Mr. R. L. Benassi, from a fresh autopsy heart of an infant (C.P., U.H. No. 864466, age 9 mos.) who died suddenly only days prior to scheduled surgical correction of her previously diagnosed ventricular septal defect. At autopsy there was severe pulmonary congestion and the cause of death was believed to be cardiac decompensation.



a FIG. 4. b FIG. 5.

FIG. 4. Exposure of the superior boundary of the ventricular septal defect at operation. a, By retraction of the septal leaflet of the tricuspid valve. b, By transection of the papillary muscles (this maneuver has not been associated with any complications in those patients in which it has been necessary for adequate exposure of the defect). It should be emphasized that the superior boundary of these defects usually does not consist of a definite margin, but rather a smooth broad roof consisting of the under surfaces of the tricuspid (septal leaflet) and mitral (aortic leaflet) valves as they insert into the atrioventricular annulus.

FIG. 5. Creation of a margin for suturing at the superior boundary of the ventricular defect. Note the precise placement of the forceps on the fibrous annulus between the insertion of the septal leaflet of the tricuspid valve and the aortic leaflet of the mitral valve. Cephalad, this margin is continuous with the aortic septum (wall of the aorta).

edge becomes fibrous in appearance as it arches upward to merge with the annulus fibrosi (atrioventricular annulus) into which the septal leaflet of the tricuspid and the aortic leaflet of the mitral valve both insert. It is at this point (their upper margin) that these ventricular defects characteristically have no definite margin or edge but rather a smooth broad roof consisting of the under surfaces of the tricuspid (septal leaflet) and mitral (aortic leaflet) valves as they insert into the atrioventricular annulus (Fig. 4). Cephalad, this annulus becomes continuous with the aortic septum (wall of the aorta).

The anatomic observation that these defects exist in three planes and frequently do not have any free margin along their superior aspect is worthy of emphasis for the surgeon because a failure to recognize this concept is quite likely to prejudice the patient's chances for a curative operation. For instance, unless care is taken to define the defect's margins as proposed, a possible misconstruction, and one which must be avoided because it will make complete closure quite impossible, is to suture a portion of the free edge of the tricuspid septa leaflet to the inferior (muscular) edge of the ventricular septal defect. This procedure will pull down a curtain of tissue over the interventricular defect and give an apparent closure, but on closer analysis it is apparent that the defect is still patulous for this leaflet tissue will constitute nothing more than a baffle interposed in the stream of the abnormal shunt from the left ventricle. Blood will still be able to circulate freely into the right ventricle as it escapes around the edges of the tricuspid leaflet. Moreover, besides failing to close the defect, the resultant deformity of the tricuspid valve will probably create a significant degree of tricuspid insufficiency. Certainly the most important step in obtaining a complete and fluid tight closure of these defects is to identify beyond question this smooth fibrous annulus at the precise point at which both the septal leaflet of the tricuspid and the aortic leaflet of the mitral valve insert into it (Fig. 4). This tissue is smooth and white in appearance resembling Cooper's ligament in a hernia repair. Then, un-

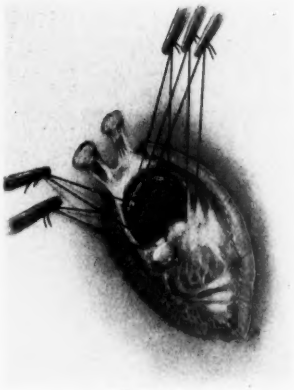
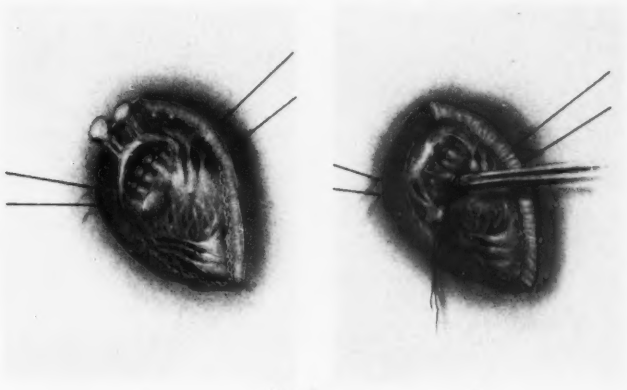


FIG. 6.



a FIG. 7. b

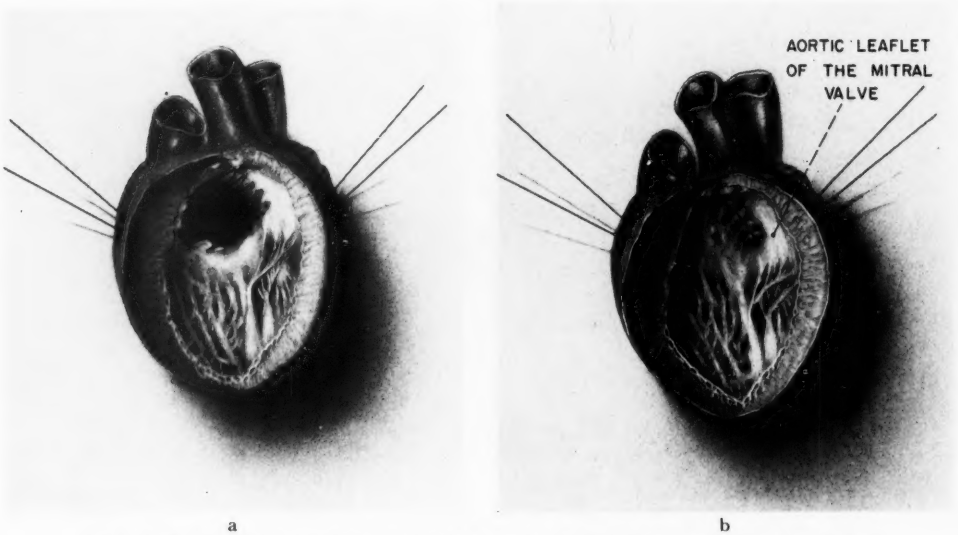
FIG. 6. The placement of interrupted silk stitches for closure of the ventricular septal defect. There is no danger of air embolism as long as the ventricular defect is open. Before tying these stitches (No. 000 silk) to close the defect, any air contained in the left ventricle is displaced by filling the latter through the defect with 5 per cent glucose in distilled water.

FIG. 7. Appearance of the ventricular defect from the right ventricle as viewed through the surgical cardiotomy. a, After closure by tying previously placed stitches. b, Repair of the transected papillary muscles of the tricuspid valve by suture.

der direct vision and with the heart empty and more flaccid one can handily create a margin at the correct place by picking up these tissues with a forceps (Fig. 5). Without the availability of direct vision for precise identification and suturing anatomic closure of these defects would scarcely seem possible.

As already noted the inferior boundary of these ventricular septal defects is the upper edge of the muscular septum. This margin of the defect is unmistakably and easily defined by its fleshy red appearance and definite margin. A valuable clue to the correct identification of the annulus between the tricuspid and mitral leaflets is to follow with the eye this easily identified inferior margin of the muscular septum posteriorly to the point where it becomes smooth and fibrous. This, then, is the area where it merges with the annulus (Figs. 4 and 5). By this method one can correctly identify the site from which to create a margin for the closure. Once this region beneath the tricuspid valve has been positively determined it can be picked up with a tissue forceps as illustrated (Figs. 4 and 5), and the remainder of the closure is readily accomplished by the placement of interrupted stitches (No. 000 silk) 3 to 4 millimeters apart (Figs. 6 and 7). Worthy of this note is the fact that at the apex of the defect the cusps of the aortic valve are usually easily recognized by their characteristic delicate translucent appearance. Thus, the first stitch at the apex of the defect immediately beneath this valve may need precise placement to achieve complete closure of the defect without injury to the aortic valve cusps. Moreover, if the defect extends directly up to the attachment of the aortic cusps it may be necessary to place this first stitch beneath the aortic valve directly through the base of the sinus of Valsalva in order to obtain a secure grasp of the aortic septum. Experimentally and clinically there has been no apparent harm from this procedure as long as the free margins of the aortic cusps remain uncompromised.

All of the stitches necessary for closure are placed first, then the left ventricle is filled with 5 per cent glucose through the defect, and the previously placed stitches are pulled up and tied. With the heart empty of blood the edges of these defects come together



a b

FIG. 8. The anatomic appearance as viewed from the left ventricle. a, Interrupted silk stitches placed for closure. b, Defect tightly closed as viewed from the left ventricular side. Note the proximity of the uppermost stitch to the cusps of the aortic valve, and the relationship of the aortic leaflet of the mitral valve to the closure.

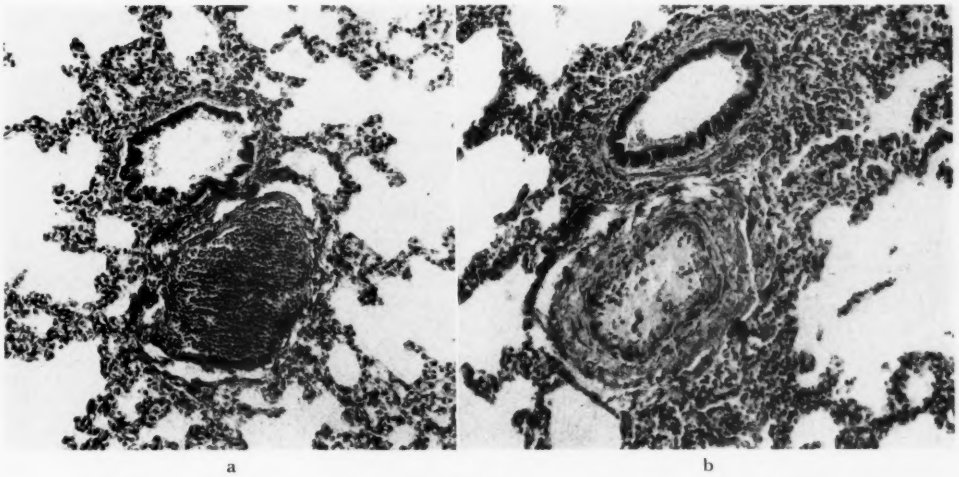
without undue tension. The left to right shunt is corrected immediately by a fluid tight closure.

As may be surmised from the foregoing description, the septal and sometimes the anterior leaflets of the tricuspid valve constitute the principle structures intruding into the surgical exposure. There are at least two feasible methods for dealing with these leaflets in order to achieve the adequate exposure necessary for the accurate placement of the stitches during closure. The first, and preferable when feasible, is to retract one or both leaflets out of the way as is shown in Figure 4a. Because of intrinsic variations in the exact position and size of these defects as well as variations in the size and position of the chordae tendineae and papillary muscles such simple retraction may not be sufficient to give adequate exposure. In that case one or more of the papillary muscles must be transected. We believe that it is better to cut the papillary muscles near their insertion rather than to divide the individual chordae because it is much easier to repair the former anatomically. Figures 4b and 5 indicate the exposure obtained by this maneuver, and Figure 7 depicts the repair of the divided papillary muscle carried out after closure of the defect in order to prevent the occurrence of any tricuspid incompetence. We have resorted to this latter procedure in 2 of these clinical cases (Cases 2 and 6) with no discernible ill effects.

Figure 8 may be helpful in presenting the appearance of the closure stitches as they would be viewed from the left ventricular side of the heart. It should be noted here again the position of the uppermost stitch in immediate juxtaposition to the aortic valve.

The cardiotomy incision has been closed in all cases with a continuous No. 000 silk stitch doubly sewn. While this closure is proceding, the coronary sinus blood flow is allowed to accumulate in the right ventricle in order to displace the remaining air. Simultaneously the anesthesiologist reinitiates pulmonary ventilation.

Air embolism. During the time that the right ventricle is open there is no danger of



a b

FIG. 9. Structural changes in the intrapulmonary arteries caused by a ventricular septal defect. a, Pulmonary arteriole from a normal 1 year old infant. Note the thin wall of the normal pulmonary arteriole. b, Pulmonary arteriole from a 1 year old infant with a ventricular septal defect (Case 1, Table II). An equivalent size artery adjacent to a similarly sized bronchus has been selected for comparison. Note the striking increase in thickness of the artery wall due to the medial hypertrophy with the consequent narrowing of its lumen.

air embolism as long as the ventricular septal defect is also open. The pressure of the blood in the aorta is sufficient to prevent any air entering from the left ventricle. The critical period occurs when the ventricular septal defect is first closed thus converting the left ventricle into a closed cavity. Therefore, before tying the stitches for closure of the septal defect the left ventricle is filled through the defect with 5 per cent dextrose in distilled water delivered via a tube connected to a pressure bottle. This maneuver effectively displaces the contained air.

RESULTS

Patients. As may be ascertained from the appended case reports 8 patients with ventricular septal defects have had their heart and lungs totally by-passed for periods of from 5 to 26½ minutes utilizing the technique of controlled cross circulation. During this interval of total by-pass each of these patients has had a right ventricular cardiotomy carried out to permit a suture closure of the ventricular septal defect under direct vision. There were 2 deaths occurring 4 and 11 days postoperatively. Both of these deaths were in infants who were desperately ill at the time of their surgery. The deaths in both of these cases were due to respiratory complications to which these patients with severe pulmonary hypertension are particularly prone. Such possible complications as complete heart block, ventricular fibrillation, air embolism, or abnormal hemorrhage have been completely absent in these 8 operations.

Of the 6 patients who have survived surgery, 4 have been recatheterized to this date and in all 4 of these patients their previously present shunts have been found to be completely corrected (Table III).

Donors. There has been no donor mortality in any of these 8 patients, nor has there been any significant donor complications. The donors have been hospitalized the afternoon prior to surgery and all have been discharged from 36 hours to 4 days postperfusion. All donors have had a retention of normal pedal arterial pulses in the limb utilized for perfusion.

CASE REPORTS

CASE 1. G. G., a male infant, 1 year of age, had spent 10 of his 12 months of life in various hospitals because of repeated attacks of pneumonia and cardiac decompensation. Cyanosis was observed in association with these episodes of pneumonia. Clinically there was a loud systolic murmur and thrill along the left sternal border. Physical growth and development had been significantly delayed, and at 1 year of age he weighed only 6.9 kilograms. He had been maintained on digitalis since early infancy. Cardiac catheterization had disclosed the presence of an interventricular septal defect with pulmonary hypertension (Table II). An older sister had died of a ventricular septal defect in 1950. Surgical operation was undertaken March 26, 1954 by means of cross circulation utilizing the father as the donor. Through a right ventricular cardiotomy a large interventricular septal defect 3 centimeters in diameter was closed by direct suture. The heart and lung were totally by-passed for 13 minutes. The operation was without incident and the patient appeared to be making a satisfactory recovery when he developed a rapidly progressing pneumonia and tracheobronchitis and died 11 days after surgery. At the necropsy, the presence of the severe respiratory complications were substantiated. The closure of the interventricular septal defect was good, but not perfect since a 4 millimeter opening still remained at the lower end of the defect where one of the stitches had not been precisely placed. The donor was discharged from the hospital in good condition 36 hours postperfusion. Figure 9 demonstrates the severe vascular abnormalities present in the pulmonary arterioles of this 12 month old patient as a consequence of his ventricular septal defect.

CASE 2. B. M., a boy, age 4 years, and weighing 16 kilograms, had had 5 previous hospital admissions for pneumonia. His exercise tolerance was poor, but there was no cyanosis. Clinically there was a loud systolic murmur and thrill along the left sternal border. His heart was proved enlarged by x-ray examination. Cardiac catheterization 2 years prior to surgery had established the presence of an interventricular septal defect (Table II). Operation by means of cross circulation was undertaken April 20, 1954 using the patient's father as the donor. Upon opening the right ventricle the operative field was found to be very bloody because of regurgitation of arterial blood back into the heart through the aortic valve rendered temporarily incompetent presumably by displacement and the collapsed state of the empty heart. In order to achieve a dry intracardiac field it was necessary as a maneuver of expediency to occlude the ascending aorta by digital compression at a site between the arterial inflow catheter and the origin of the coronary arteries while the stitches were placed in the margins of the ventricular defect. Also, in order to obtain adequate exposure of the boundaries of the defect it was necessary to transect the anterior papillary muscle of the tricuspid valve. Despite these added difficulties, the rhythm of the heart remained regular throughout the entire procedure. The ventricular defect was closed by interrupted silk sutures, the papillary muscle was resutured, and the cardiotomy closed. The cardiac inflow was occluded for a total of 26½ minutes and the patient was supported by the pump for a total of 27½ minutes. The immediate postoperative convalescence was delayed by the occurrence of a pneumonitis, but the patient recovered and was discharged in good condition. He still has a soft systolic murmur without a thrill. The donor was discharged in good condition 4 days postperfusion. The donor in this case was kept in the hospital for 2 additional days because of a fever which was due to a phlebitis in the saphenous vein distal to the point of ligature.

CASE 3. P. S., a 5 year old girl, weighing 14.5 kilograms, had had an extremely difficult preoperative life due to repeated bouts of pneumonia and decompensation. Her parents had lost count of the number of her hospital admissions. During one of these admissions she had spent 7 months continuously in an oxygen tent because of severe dyspnea and cyanosis with cardiac decompensation. Cardiac catheterization 4 years prior to surgery had established the presence of a ventricular septal defect with pulmonary hypertension (Table III). She was not cyanotic at rest at the time of surgery. She was receiving digitalis at the time of surgery. Surgical operation was undertaken April 23, 1954 using her father as the donor. A large (3.0 centimeter in diameter) ventricular septal defect was closed under direct vision without incident. The heart was open for 10½ minutes. Immediately following closure of the cardiotomy and release of the venae cavae it was noted that the auricular and ventricular beats of the heart were out of phase. Ten minutes later, without special treatment, the cardiac rhythm was completely normal. Convalescence was uncomplicated. The patient's preoperative harsh systolic thrill and murmur have completely disappeared. The donor was discharged in good condition 4 days after the perfusion. The 2 additional hospital days were due to a superficial saphenous phlebitis in the vein distal to the ligature.[9] Recatheterization was performed 4 months postoperatively and her defect found to be completely closed (Table III). It may be noted that her pulmonary pressures have not yet returned to normal. There has been a significant regression in the appearance of her pulmonary vasculature in the roentgenogram (Fig. 10). In the 12 months since surgery she has grown 3½ inches in height and gained 17 pounds in weight.

CASE 4. L. T., a 9½ month old infant, had had 3 previous hospital admissions for pneumonia. An interventricular septal defect had been proved by cardiac catheterization (Table III). The heart was consider-

[9]This complication has been avoided in subsequent cases by resuturing the saphenous vein to restore continuity rather than ligating after removal of the venous catheter.

a b

FIG. 10. Thoracic roentgenograms from patient P.S. (Case 3, Table III) before and after closure of a ventricular septal defect. a, Before. b, Four months after operation. Note the diminution in vascularity of the lung fields in the film taken postoperatively.

ably enlarged and the child had been digitalized. Repair of the ventricular septal defect was undertaken May 18, 1954 by means of cross circulation utilizing the father as the donor. Closure of the defect (1.7 cm.) was without special incident. The venae cavae were occluded for 8¼ minutes. Convalescence was uncomplicated. The systolic cardiac murmur and thrill completely disappeared. The donor was discharged 36 hours after perfusion. Cardiac recatheterization 5 months after surgery demonstrated complete closure of the septal defect (Table III). Some elevation of the pulmonary pressures still remained at the time of this recatheterization study.

CASE 5. T. F., a male infant, 1 year of age, in whom a heart murmur was first noted on the second day of life suffered from repeated respiratory infections. There had been 3 hospitalizations for pneumonia despite prophylactic antibiotics. His physical development was delayed. Digitalis therapy had been started previously.

There was a loud systolic thrill and murmur noted along the left sternal border. Cardiomegaly was noted in the roentgenogram with a significant shift of the heart into the left chest. Cardiac catheterization disclosed the presence of a ventricular septal defect with pulmonary hypertension (Table II). On June 8, 1954 the ventricular septal defect was closed by suture under direct vision without incident. However, upon entering the chest for this operation the left lung was found to be completely atelectatic and although the heart and greatly enlarged pulmonary artery were noted to undergo a striking decrease in size immediately after closure of the ventricular defect it was still not possible to obtain any expansion of this lung at the time of surgery using intrapulmonic pressures as high as deemed safe. The infant's initial postoperative course was satisfactory despite this added complication.

During the night of the fourth postoperative day, however, the patient died suddenly. Autopsy disclosed the fact that death was due to an atelectasis of the remaining functioning (right) lung caused by a mucus plug in the right main bronchus. Microscopic analysis of this lung showed very severe intimal and medial arteriolar changes. The ventricular septal defect was completely closed. At autopsy it was also evident that the complete atelectasis of the left lung was due to the prolonged pressure of the greatly en-

larged pulmonary artery upon the left main bronchus.[10] The finding of severe intimal pulmonary arteriolar proliferation in this infant only 12 months of age was surprising and undoubtedly was a significant factor contributing to his demise.

CASE 6. C. L., a female infant, age 1 year, weighing only 5 kilograms, did poorly from the time of birth (feeding problem, delayed growth, repeated bouts of pneumonia). A typical systolic murmur and thrill with cardiomegaly were present. Cardiac catheterization disclosed a ventricular septal defect with pulmonary hypertension (Table III). This infant had been previously digitalized by the referring cardiologist, and she had been hospitalized elsewhere continuously for the 3 months prior to referral to the University Heart Hospitals for surgical treatment because it was not deemed likely that she could survive outside of a hospital. Neither of the parents had blood compatible with that of the patient. For this reason a distant relative was utilized as the donor for the closure of the patient's ventricular septal defect on July 23, 1954. The child's postoperative convalescence was uncomplicated. The murmur and thrill have completely disappeared since surgery. The donor was discharged 36 hours postperfusion. Digitalis therapy was discontinued 4 weeks after surgery. Since surgical correction of her ventricular defect this baby has shown a remarkable spurt in development. In the first 6 months after surgery her weight increased from 11½ pounds to 20 pounds. When she returned for cardiac catheterization 6 months after surgery it was found that her defect was completely closed and the pulmonary pressures were now normal (Table III).

CASE 7. K. H., a girl, age 5 years, weighing only 11.4 kilograms, exhibited delayed growth obvious early in infancy and a diagnosis of congenital heart disease was made at the age of 3 months. Her first 2 years of life were complicated by frequent prolonged episodes of lung congestion and pneumonia. At 2 years there was an unsuccessful attempt at cardiac catheterization and then an exploratory thoracotomy for a possible patent ductus was carried out but none was found. The surgeon concluded that she had an interventricular septal defect. At that time she was started on digitalis because of cardiac decompensation and terramycin daily as prophylaxis against respiratory infections. Her growth continued to be very slow. At age 5 years she was referred to the University Heart Hospital for cardiac catheterization, and this procedure disclosed an interventricular septal defect with severe pulmonary hypertension (Table III). There was a grade 4 systolic murmur and thrill along the left sternal border with very prominent forward bowing of the chest due to cardiomegaly. Corrective surgery by the cross circulation technique was performed July 30, 1954. At operation, in addition to a large (2.5 cm.) ventricular defect in the membranous area of the septum, there were 2 additional (4 millimeters in diameter) defects in the muscular septum. All of these abnormal openings were sutured with interrupted No. 000 silk stitches. The convalescence was uncomplicated. At the time of discharge a soft systolic murmur (grade 1) could be heard, but no thrill palpated. Digitalis and the antibiotics were discontinued shortly after surgery. Since her operation she has done very well, gaining 5 pounds in weight, 1¾ inches in height in the first 6 months and her mother indicates that the child has a "sparkle and vivaciousness never apparent before." The donor's convalescence was uncomplicated and he was discharged 3 days after the perfusion. Recatheterization of this child 9 months after the curative surgery indicated that the shunt had been completely corrected and that the previously present severe pulmonary hypertension had returned to normal levels (Table III). This finding is significant because not only did this child have multiple ventricular defects, but her lung biopsy taken at the time of surgery disclosed marked narrowing of the pulmonary arterioles due to medial hypertrophy without intimal proliferation.

CASE 8. M. G., a female infant, was 5 months old at the time of surgery. At 3 weeks of age she had been hospitalized because of feeding difficulties, failure to gain weight, dyspnea, and pneumonia. At rest she was mildly cyanotic, and upon crying (which was abnormally weak) cyanosis was definite. Cardiomegaly was present. The femoral pulses were strong. The infant was digitalized at the age of 8 weeks. A grade 4 systolic murmur and thrill were present along the left sternal border. Cardiac catheterization (Table II) confirmed the clinical diagnosis of a ventricular septal defect. The severe pulmonary hypertension was considered an ominous sign and corrective surgery was performed August 13, 1954 utilizing the mother as the donor. Though the defect was large (the size of a dime) the closure proceded smoothly. For 12 minutes after release of the venae cavae following closure of both the defect and the cardiotomy the auricles beat at a rate of 100 per minute and the ventricles at a rate of 50 per minute. Then normal rhythm spontaneously returned and remained thereafter. During this brief interval of a 2.1 heart block the pump was allowed to run in support of the heart even though the venae cavae had been released. Postoperatively the murmur and thrill have completely disappeared. The infant's immediate convalescence was uncomplicated although she showed a tendency to gain weight abnormally unless salt was restricted. She was discharged on the seventeenth postoperative day in apparently good

[10]This same mechanism (pulmonary artery enlargement) is responsible also for the left recurrent laryngeal nerve paralysis (manifested by their weak cry) that many of these patients have. This paralysis undoubtedly contributes in part to the susceptibility to respiratory complications of these patients with pulmonary hypertension even after the primary defect has been completely corrected. The other important factor contributing to the postoperative susceptibility of these patients to respiratory complications is the fact that the pulmonary hypertension and other abnormalities in the lungs persist for some time after the curative heart surgery.

condition. In the 8 months since surgery this child has gained considerably but she has not shown the dramatic improvement which has characterized the postoperative course of the other 5 survivors. The baby has continued to be troubled by repeated respiratory infections. Moreover, the heart has remained unchanged in size and digitalis has been required. Cardiac ausculation and palpation reveal neither murmur nor thrill. The referring cardiologist believes that this infant also has an associated congenital fibroelastosis of the left ventricle.

DISCUSSION

In the past, there has been little question of the desirability of closing ventricular septal defects particularly those associated with pulmonary hypertension. The main barrier to the performance of curative surgery for these septal defects has been the lack of a method for working within the ventricle of the open heart under direct vision in an unhurried manner.

Previously reported attempts to close ventricular septal defects by indirect or "blind" methods have been associated with a high operative mortality and none of the few survivors has achieved closure of the defect as evidenced by postoperative follow-up studies. In our opinion the complex anatomic relationships of the usual type of ventricular defect makes closure attempts by blind methods injudicious. In the one reported attempt at closure of a ventricular septal defect by open cardiotomy utilizing venous inflow stasis and hypothermia (supplemented by intra-arterial transfusions) the patient survived the operation, but closure of the defect was not possible. None of the patients with ventricular septal defects operated upon to date utilizing pump oxygenators has survived the operative procedure.

We would emphasize the fact that the use of hypothermia alone or in combination with other methods as suggested by some is detrimental to success for intraventricular procedures because of the crippling effects of reduced temperature upon the cardiac conduction mechanism.

The technique of controlled cross circulation by providing a practicable method for direct vision intracardiac surgery for prolonged periods of time has removed this barrier confronting cardiac surgeons and has made curative surgery for ventricular septal defects possible for the first time as evidenced by the patients herein reported.

In these intracardiac repairs utilizing cross circulation the complete absence of a number of the predicted complications and dangers of operating upon the ventricular septum under direct vision such as complete heart block, ventricular fibrillation, and air embolism has been gratifying. The freedom from cardiac conduction disturbances confirms the experimental observations (5, 7, 14, 15) that when the myocardium is normothermic, is relieved of its pumping burden, and is well oxygenated by a continuance of some coronary arterial flow there is little likelihood of serious cardiac conduction difficulties developing even during the placement of numerous stitches in the ventricular septum for closure of these defects. These observations would seem to deny the classical concept that the conduction system of the human or canine heart (atrioventricular node and bundle of His) is concentrated in a small localized discrete locus which is thereby very vulnerable to mechanical injury.

The absence of any appreciable hemolysis, as well as the freedom from abnormal postoperative bleeding confirm the lack of significant damage to the patient or donor's clotting mechanism and also substantiate the advantages gained by the practice of discarding the highly hemolyzed blood aspirated from the interior of the heart rather than returning it to the patient.

No deaths occurred during or even shortly after these operative procedures despite the poor preoperative condition of most of the patients. This observation offers ample testimony to the physiologic soundness of this particular method for intracardiac surgery and augurs well for the future of this entire field. The demonstration that right ventricular cardiotomy and septal suture can be successfully performed even in seriously ill patients should dispel much of the discour-

agement previously prevalent in this field and stimulate further rapid developments in the application of direct vision intracardiac corrective surgery to congenital and acquired cardiac pathology.[11]

The ventricular defects have been found to be completely closed in all 4 of the patients recatheterized, and it is particularly significant that in 2 of these 4 patients the pulmonary pressures have returned to normal in the relatively short interval (4 to 9 months) between surgical correction of the defect and the recatheterization studies. Such a finding is gratifying in view of available experimental observations which have indicated that when the inciting factor for pulmonary hypertension is removed under controlled conditions, the vascular changes have not appreciably regressed within the same period of time that was required for their development (8). However, neither did further progression of these vascular changes occur in the experimental studies mentioned. Moreover, these studies were carried out in adult dogs who had achieved their full growth. The potential remaining for further growth of the pulmonary vessels may be a most important consideration in this regard.

Pertinent clinical observations in patients with pulmonary hypertension secondary to patent ductus arteriosus have justified a certain amount of optimism that a gradual regression of the pulmonary hypertension may occur even in adults following surgical correction of the shunt. We have believed that the prognosis in children would certainly be still more optimistic since additional improvement could be anticipated upon the basis of the growth potential remaining for their pulmonary vessels. The evidence from these patients herein reported would seem to corroborate this latter viewpoint.

However, at present, the problem remains unsolved for those individuals in whom the vascular changes have progressed to a point where the pulmonary resistance is incompatible with immediate survival after correction of their defect. This consideration undoubtedly deserves emphasis both for the diagnostician in deciding when to undertake precise diagnostic studies in a particular patient as well as for the surgeon in selecting the optimum time for the surgical correction.

Although the operative risk for this type of major surgery is probably greater in seriously ill infants, the fact that more than one-half of all individuals dying with a ventricular septal defect succumb before 1 year of age indicates that not only is corrective surgery for this condition feasible in infancy, but is virtually mandatory in deteriorating infants if one's objective is to save lives.

[11]Since submission of this manuscript Kirklin and associates have reported (*Proc. Mayo Clin.*, 1955, 30: 201) the closure of ventricular septal defects in 5 patients with 2 survivors using the Gibbon type pump-oxygenator.

SUMMARY AND CONCLUSIONS

1. Controlled cross circulation by providing a reliable method for excluding the heart and lungs from the circulation for prolonged periods of time has removed the barrier to direct vision access to the interior of the heart for curative surgical procedures.

2. This technique for total by-pass of the heart and lungs consists of the simultaneous reciprocal exchange of equal quantities of compatible blood from the arterial system of the donor to the patient's arterial circulation, and from the caval system of the patient to the veins of the donor individual.

3. The essential functions of the donor circulation are to oxygenate and revitalize the venous blood received from the patient.

4. A pump is essential to control accurately this continuous interchange of blood between the patient and donor.

5. Technical considerations in the clinical application of cross circulation are described in detail with particular reference to the cannulations, anesthesia, and selection of compatible donors.

6. Eight patients, all seriously ill with ventricular septal defects, cardiomegaly, and pulmonary hypertension, have had their circulatory systems linked with a suitable donor; their heart and lungs totally bypassed, and a right ventricular cardiotomy

carried out to permit direct vision suture closure of their ventricular septal defects.

7. All of these clinical operations have been carried out at normal body temperatures to obviate the deleterious effects of reduced temperature upon the cardiac conduction system.

8. The heart and lungs in these 8 patients were totally by-passed from 5 to 26½ minutes during which time the patient's body was perfused at reduced rates of flow based upon the azygos flow experimental studies.

9. These reduced rates of blood flow have been demonstrated to be safe for man and the simplifications made feasible by the recognition of this concept have contributed immeasurably to the safety and success of direct vision intracardiac surgery.

10. There were 2 deaths in these first 8 patients. Both deaths were in infants and occurred during the convalescent period (4 days and 11 days postoperatively respectively) from respiratory complications which these patients with severe pulmonary hypertension are particularly susceptible.

11. There has been no patient mortality attributable to the cross circulation method of total cardiac by-pass per se. Once the circulatory systems of the patient and donor have been linked together the patient has been assured of a continuous supply of oxygenated and otherwise perfectly adjusted blood from the donor.

12. Conduction systems disturbances such as ventricular fibrillation or persistent complete heart block have not occurred even though all defects have been closed by direct sutures placed in the ventricular septum with no effort made to avoid the "so-called" vulnerable areas. This fact verifies for man our experimental observations indicating that the heart euthermic and totally by-passed to reduce its work load needs only a very reduced coronary arterial flow to remain well oxygenated; and further, such a heart becomes very resistant to the induction of arrhythmias. These observations constitute important additions to basic knowledge of cardiac surgical physiology.

13. The complete absence of such possible complications as air embolism, excessive hemolysis, or postoperative hemorrhage has been gratifying.

14. Four of the first 6 surviving patients have been recatheterized 4 to 9 months after closure of their ventricular septal defects and in all 4 patients the septal defect has been found to be completely corrected. No shunt remains. In 2 of these patients the pulmonary pressures have already returned to normal levels. One of these 2 patients with normal postoperative pressures, K. H., Case 7, is particularly significant because prior to curative surgery she had had a remarkable inhibition of body growth and a severe pulmonary hypertension with marked pulmonary arteriolar narrowing caused by multiple (3) ventricular defects. The other 2 patients were found to have pulmonary pressures that were still elevated above normal levels, but less than preoperative levels.

15. These 4 patients represent the first to have successful complete correction of ventricular septal defects as evidenced by disappearance of murmurs, thrills, and objective postoperative catheterization studies demonstrating absence of the previously present shunt.

16. There was no mortality nor complications of any significance among these 8 donors.

REFERENCES

1. ANDREASEN, A. T., and WATSON, F. Experimental cardiovascular surgery, "the azygos factor." Brit. J. Surg., 1952, 39: 548–551.
2. Idem. Experimental cardiovascular surgery; discussion of results so far obtained and report on experiments concerning a donor circulation. Brit. J. Surg., 1953, 41: 195–206.
3. BLUM, L., and MEGIBOW, S. J. Exclusion of the dog heart by parabiosis. J. Mount Sinai Hosp., N. York, 1950, 17: 38–43.
4. COHEN, M., HAMMERSTROM, R. N., SPELLMAN, M. W., VARCO, R. L., and LILLEHEI, C. W. The tolerance of the canine heart to temporary complete vena caval occlusion. The Surgical Forum, 1952; The American College of Surgeons. Pp. 172–177. Philadelphia: W. B. Saunders, 1953.
5. COHEN, M., and LILLEHEI, C. W. Autogenous lung oxygenator with total cardiac by-pass for intracardiac surgery. The Surgical Forum, 1953; The American College of Surgeons. Pp. 34–40. Philadelphia: W. B. Saunders, 1954.

6. Idem. A quantitative study of the "azygos factor" during vena caval occlusion in the dog. Surg. Gyn. Obst., 1954, 98: 225–232.
7. Cohen, M., Warden, H. E., and Lillehei, C. W. Physiologic and metabolic changes during autogenous lobe oxygenation with total cardiac by-pass employing the azygos flow principle. Surg. Gyn. Obst., 1954, 98:523–529.
8. Ferguson, D. J., and Varco, R. L. The relation of blood pressure and flow to the development and regression of experimentally induced pulmonary arteriosclerosis. Circulation Res., 1955, 3: 152–158.
9. Glenn, W. L. W., and Sewell, W. H., Jr. Experimental cardiac surgery—IV, the prevention of air embolism in open heart surgery; repair of interauricular septal defects. Surgery, 1953, 34: 195–206.
10. Kerr, E., Davis, C., Woolsey, J., Grimes, O., Stephens, H., Byron, R., and McCorkle, H. J. The maintenance of circulation by cross transfusion during experimental operations on the open heart. The Surgical Forum, 1951; The American College of Surgeons. Pp. 222–229. Philadelphia: W. B. Saunders, 1952.
11. Landsteiner, K. Zur Kenntnis der Antifermentativen, Lytischen, und Agglulinerenden Wirkungen des Blutserums und der Lymphe. Zbl. Bakt., 1900, 27: 357–362.
12. Lillehei, C. W. Controlled cross circulation for direct vision intracardiac surgical correction of interventricular, atrioventricular communis, and tetralogy of Fallot defects. Postgraduate M., 1955, 17: 388–396.
13. Southworth, J. L., and Pierce, E. C. Cross circulation for intracardiac surgery. Arch. Surg., 1952, 64: 58–63.
14. Warden, H. E., Cohen, M., DeWall, R., Schultz, E., Buckley, J. J., Read, R. C., and Lillehei, C. W. Experimental closure of interventricular septal defects and further physiologic studies on controlled cross circulation. The Surgical Forum, 1954; The American College of Surgeons. Pp. 22–28. Philadelphia: W. B. Saunders, 1955.
15. Warden, H. E., Cohen, M., Read, R. C., and Lillehei, C. W. Controlled cross circulation for open intracardiac surgery. J. Thorac. Surg., 1954, 28: 331–343.

STUDIES OF FIBRINOGEN AND OTHER HEMOSTATIC FACTORS IN WOMEN WITH INTRAUTERINE DEATH AND DELAYED DELIVERY

JACK A. PRITCHARD, M.D., Dallas, Texas, and OSCAR D. RATNOFF, M.D., Cleveland, Ohio

SINCE THE OBSERVATIONS of Weiner, Reid, Roby, and Diamond, it has been recognized that serious hemorrhage due to alterations in the blood clotting mechanisms may occur in association with the prolonged intrauterine retention of a dead fetus. Immediately following delivery, there may be excessive bleeding from the reproductive tract. Less frequently, bleeding from other sites may take place. The principal defect seems to be a critical reduction in the concentration of fibrinogen in the circulating blood.

Fibrinogenopenia may also complicate amniotic fluid embolism or premature separation of the placenta. In these conditions, the process of fibrinogen depletion is thought to be fulminating. On the other hand, there is evidence that the fall in the concentration of fibrinogen in the case of retention of a dead fetus need not occur as rapidly as in amniotic fluid embolism or premature separation (7). Because fibrinogenopenia is common to all 3 syndromes, some confusion exists regarding the treatment of patients who do not deliver promptly after intrauterine fetal death. The present report concerns studies of the natural history of patients with this condition with particular reference to the clotting mechanism. Based upon this experience, a method of management will be described.

From the Departments of Obstetrics and Gynecology, and Medicine, School of Medicine, Western Reserve University, and University Hospitals, Cleveland, Ohio.

This work was supported in part by a research grant (P.H.S. No. H1661C) from the National Heart Institute of National Institutes of Health, Public Health Service, and by a research grant from the Cleveland Area Heart Society.

METHODS

Studies of the concentration of fibrinogen in plasma were made in a total of 31 patients who remained undelivered 3 or more weeks after apparent intrauterine fetal death. Wherever possible, serial determinations were made before, during, and after labor and delivery. In these laboratories, the concentration of fibrinogen in the plasma of 36 normal nonpregnant women averaged 294 milligrams per 100 milliliters, ranging from 164 to 485 milligrams per 100 milliliters, with a standard deviation of the mean of 58.8. Hypofibrinogenemia was thought to exist when the plasma concentration was less than 150 milligrams per milliliters. In several cases, the platelet count, bleeding time, tourniquet test, clotting time in plain and silicone-coated glass tubes, plasma fibrinolytic activity, and apparent and true plasma prothrombic activities were determined. The term "apparent" plasma prothrombic activity refers to the per cent prothrombin determined by a one stage method. "True" plasma prothrombic activity refers to the per cent prothrombin determined by a one stage method in which excesses of fibrinogen, proconvertin, and proaccelerin are added to the plasma to be tested. The fibrinolytic property of amniotic fluid was tested by observing the clots formed by mixing equal volumes of amniotic fluid, normal oxalated plasma and either 0.025 M calcium chloride or bovine thrombin solution (5), and by mixing 0.1 milliliter of amniotic fluid with 0.1 milliliter of bovine thrombin solution and 0.3 milliliter

TABLE I.—SUMMARY OF STUDIES OF FIBRINOGEN LEVELS IN 23 WOMEN WHO DID NOT DEVELOP HYPOFIBRINOGENEMIA FOLLOWING INTRAUTERINE FETAL DEATH 3 TO 11 WEEKS BEFORE DELIVERY

Patient	*Gestation when expired, weeks*	*Interval until delivery, weeks*	*Labor and delivery*	*Remarks*	*Fibrinogen levels following death*	
					weeks	*mgm./100 ml.*
J.Ha.	19	4	Spontaneous		4	302
V.C.	22	8	Pitocin induction	Rh antibodies	6	536
					7	498
					8	456
B.S.	24	7	Spontaneous		5	431
					6	424
					7	360
C.R.	30	7	Spontaneous		7	276
J.Th.	18	6	D&C	Rh antibodies	6	231
J.Ta.	32	3	Spontaneous	Essential hypertension	3	447
F.M.	15	7	Spontaneous		7	450
A.E.	34	3	Spontaneous		3	652
M.H.	21	6	Spontaneous		6	382
G.We.	27	9	Spontaneous		9	424
D.I.	25	9	Pitocin stimulation	Rh negative	7	512
					9	457
M.M.	18	11	Spontaneous		11	364
E.Wo.	23	8	Laparotomy	Abdominal pregnancy	6	536
					7	558
					8	382
J.K.	32	4	Spontaneous		3	532
					4	408
J.Hu.	36	3	Spontaneous		3	416
E.Wa.	32	5	Spontaneous	Diabetes	5	397
G.Wa.	34	3	Spontaneous		3	615
J.G.	24	7	Spontaneous	Rh antibodies	2	440
					3	426
					4	412
					5	345
					6	316
					7	273
H.L.	14	10	D&C		10	374
B.M.	12	8	Spontaneous		8	472
M.Hu.	27	5	Spontaneous	Rh antibodies	2	476
					3	526
					4	438
					5	414
I.K.	12	9	D&C		9	244
M.O.	29	4	Spontaneous		4	416

of bovine fibrinogen solution. The solution of thrombin contained 10 National Institutes of Health units per milliliter, and the solution of fibrinogen contained approximately 300 milligrams of coagulable protein per 100 milliliters. As a control, barbital-saline buffer was substituted for the amniotic fluid. Other methods employed have been described previously (5).

OBSERVATIONS

In 23 patients in whom fetal death appeared to have taken place between the twelfth and thirty-sixth week of gestation, and the dead fetus had been retained in utero for 3 to 11 weeks, no evidence was found of a critical depletion of circulating fibrinogen (Table I). The concentration of fibrinogen at delivery ranged from 231 to 652 milligrams per 100 milliliters of plasma. In 7 of these patients serial fibrinogen determinations were made for several weeks following intrauterine death; in all 7 there was evidence of a progressive reduction in the concentration of circulating fibrinogen. The decrease occurred in roughly linear fashion, but the concentration of fibrinogen at no time reached a level lower than that in the normal nonpregnant woman.

During this same period of time, 8 cases of prolonged intrauterine retention of a dead fetus were encountered in which the fibrinogen level was dangerously low. In 3 instances, hemorrhagic manifestations

prompted studies of the fibrinogen concentration in the patients' plasmas. In the other 5 cases the hypofibrinogenemia was discovered in a routine study of patients with intrauterine retention of a dead fetus. Serial measurements of circulating fibrinogen in 3 of these 5 patients revealed a progressive decrease in its concentration until hysterotomy was performed (Case 2, Fig. 2) or vaginal delivery occurred (Case 1, Fig. 1a and b, Table II, and Case 3, Fig. 3).

CASES DEMONSTRATING ABNORMALLY LOW CIRCULATING FIBRINOGEN

CASE 1. Mrs. J. (U.H. No. 176-801), pregnant for the sixth time and with 4 living children, was Rh negative and Rh isosensitized. Intrauterine death occurred at 31 weeks' gestation. Prior to this and during the following 9 weeks until the onset of labor the patient was asymptomatic except for moderate bleeding from the gums. Similar gingival bleeding had been noted during her previous pregnancies.

Starting 3 weeks after the cessation of fetal movements blood studies at weekly intervals were carried out. Included in the studies were measurements of plasma fibrinogen, fibrinolytic activity, platelets, bleeding times, capillary fragility, clotting times in plain and in silicone-coated glass tubes, apparent and true plasma prothrombin activity, and hematocrit.

As shown in Figure 1a, initially there was a gradual progressive fall in the concentration of plasma fibrinogen until the seventh week after intrauterine death, but during the next 2 weeks there was a much more marked rate of decrease. By the ninth week it had dropped to 116 milligrams per 100 milliliters. During this same period of time none of the other hematologic studies revealed any abnormality except for the plasma prothrombic activity (Table II). By the ninth week following fetal death the apparent prothrombic activity was 45 per cent of normal; the true prothrombic activity, however, was 84 per cent of normal at this time. The concentration of platelets appeared to drop somewhat but the platelet count never was noted to be abnormally low. Clotting times of blood in both plain and silicone-coated glass tubes remained normal as did the fibrinolytic activity of the plasma.

The patient was admitted the day after the plasma fibrinogen level was found to be 116 milligrams per 100 milliliters. After repeating all of the blood studies listed, 2.2 grams of human fibrinogen were given intravenously in 550 milliliters of isotonic saline solution during a period of 18 minutes. Four minutes after the completion of the infusion the plasma fibrinogen concentration was 182 milligrams per 100 milliliters compared to a preinjection level of 118 milligrams per 100 milliliters (Fig. 1b). Within 18 hours the plasma concentration returned to the preinjection range. At this time labor started spontaneously. During the next 1½ hours labor progressed satisfactorily but following artificial rupture of the bulging amniotic sac the cervix was noted to be dilated about 4 centimeters. Uterine contractions became more brief and somewhat irregular so an intravenous infusion of diluted pitocin was given to re-establish and maintain effective uterine contractions. Three hours after the onset of labor and 1 hour after the start of the pitocin infusion the plasma fibrinogen concentration was 117 milligrams per 100 milliliters. During the 2 hours prior to delivery there was moderately excessive but not alarming blood loss from the vagina.

Delivery of the macerated fetus and the placenta occurred spontaneously 5 hours after the onset of labor and 3 hours after the start of the pitocin infusion. The plasma fibrinogen concentration 6 minutes after the delivery of the fetus and 1 minute after delivery of the placenta was 104 milligrams per 100 milliliters.

At the onset of labor the platelet concentration was 181,000 per cubic millimeter and 6 minutes after delivery was 172,000 per cubic millimeter. The clot lysis time, which prior to the onset of labor had never been found to be shorter than 2 days, was 12 hours in blood obtained immediately after delivery of the placenta.

During the first 6 hours after parturition the pitocin infusion was continued to insure a well contracted myometrium. Blood loss during this time was minimal.

One hour after delivery the fibrinogen level was 113 milligrams per 100 milliliters and the clot lysis time was 12 hours. Four and one-half hours and 13½ hours after delivery the plasma fibrinogen concentrations were 135 and 156 milligrams per 100 milliliters, respectively. Within 4½ hours after delivery the clot lysis time had returned to the prepartum value of 2 days. The fibrinogen concentration continued to increase, reaching 212 milligrams 27 hours after delivery and 272 milligrams 4 days after delivery. A bilateral partial salpingectomy was carried out without incident on the third postpartum day. Although neither intravenous fibrinogen nor whole blood therapy had been used during labor, delivery, or the postpartum period, the hematocrit never fell below 42.

CASE 2. Mrs. C. (U.H. No. 630870), Rh negative, but without demonstrable anti-Rh antibodies, pregnant for the fifth time and with 4 living children, last felt fetal movement at 26 weeks' gestation. Three weeks later, a serial study of the patient's plasma fibrinogen concentration was begun. During the next 5½ weeks, there was a progressive and nearly linear fall from an initial concentration of 255 milligrams per 100 milliliters to 118 milligrams per 100 milliliters. The patient remained asymptomatic and no other laboratory evidence suggestive of a possible hemorrhagic state was obtained. The platelet count was 172,000 per cubic millimeter, and the clot lysis time was normal. Two grams of fibrinogen were given intravenously and the patient's plasma fibrinogen concentration was studied

TABLE II.—SERIAL STUDIES OF THE HEMOSTATIC MECHANISMS IN CASE I

Weeks fetus dead	*Fibrinogen, mgm./100 ml.*	*Clot lysis time**	*Platelets, cu.mm.*	*Prothrombin, —per cent normal— Apparent*	*True*	*Clotting time, —minutes— Glass**	*Silicone**
3	478	—	—	—	—	—	—
4	462	—	—	—	—	—	—
5	430	—	—	—	—	—	—
6	395	—	220,000	—	—	32	111
7	385	4 days	257,000	89	—	36	136
8	265	—	—	55	96	—	—
9	116	2 days	—	45	84	29	106
Fibrinogen Rx							
Preinjection	118	2 days	154,000	45	84	33	—
+4 min.	182	—	—	42	70	30	—
+2 hours	150	3 days	—	47	82	—	—
+5 hours	148	3 days	—	—	—	—	—
+18 hours (early labor)	113	30 hours	181,000	45	82	—	—
+21 hours	117	—	—	48	96	—	—
+23 hours (6 min. after delivery)	104	12 hours	172,000	42	82	—	—
Postpartum							
+1 hour	113	12 hours	—	47	86	32	—
+4 hours	135	2 days	—	55	94	—	—
+11 hours	156	—	—	65	110	—	—
+27 hours	212	—	—	—	—	—	—
+2 days	213	—	—	—	—	—	—
+4 days	272	—	—	—	—	—	—
+30 days	266	—	—	—	—	—	—

*Normal values: Clot lysis time 2 days or longer except for the recently delivered patient in whom it frequently is shorter; glass clotting time 31 minutes (S.D.± 9.9); silicone clotting time 103 minutes (S.D.± 19.5) (7).

repeatedly. Within 72 hours, the concentration of circulating fibrinogen had returned to the preinjection value. Following failure of induction of labor with pitocin 3.5 grams of fibrinogen were administered just before abdominal hysterotomy. These procedures were followed by prompt restoration of the plasma fibrinogen concentration to normal. A large hematoma of the abdominal wall at the site of the incision complicated the postoperative period, but following its drainage the patient's course was unremarkable. The fibrinogen studies are summarized in Figure 2.

Case 3. Mrs. B. (U.H. No. 613988), Rh positive, pregnant for the fourth time but with no living children, felt fetal movements only briefly for about 2 weeks before the twentieth week of gestation. Six and one-half weeks later blood studies were begun. At this time, the plasma fibrinogen concentration was 147 milligrams per 100 milliliters, platelets were 146,500 per cubic millimeter, the clotting times in glass and silicone-coated tubes were normal, and the clot lysis time was longer than 24 hours. The patient remained asymptomatic except for a slight nosebleed 2 days after these studies were made, at a time when the concentration of fibrinogen had fallen to 117 milligrams per 100 milliliters, the platelets were 176,000 per cubic millimeter, the clotting times were normal, and the clot lysis time was 2 days. With fibronogen and compatible blood readily available, labor was induced and maintained, first with repeated intramuscular injections of pitocin, and then with an intravenous infusion of pitocin diluted with aqueous dextrose solution. After 7 hours the fetus and placenta were delivered spontaneously without excessive blood loss; although no fibrinogen or blood was given, the hematocrit on the third day post partum was 45. The plasma fibronogen concentration and platelet count 20 minutes after delivery were 127 milligrams per 100 milliliters and 172,000 per cubic millimeter respectively, and the clot lysis time was 2 days. Following delivery there was a rather rapid rise in the plasma fibrinogen concentration (Fig. 3). The patient's recovery was uneventful.

Case 4. E. M. (U.H. No. 296-417), pregnant for the fourth time but having only 1 living child, was Rh positive. The uterus increased in size normally until about 16 weeks after the last menstrual period. No further growth was noted nor was fetal motion felt during the next 3 months. Otherwise the patient was asymptomatic.

At the end of this 3 month period studies of the hemostatic mechanism were carried out. The plasma fibrinogen concentration over a 5 day period ranged from 117 to 133 milligrams per 100 milliliters, the platelet count was 154,000 per cubic millimeter, the apparent plasma prothrombic activity was 87 per cent of normal, the clotting times of blood in plain glass and in silicone-coated glass tubes were normal, and the clot lysis time of recalcified plasma ranged from overnight to 3 days.

The patient was admitted to the hospital and 3 grams of fibrinogen were given intravenously. This resulted in

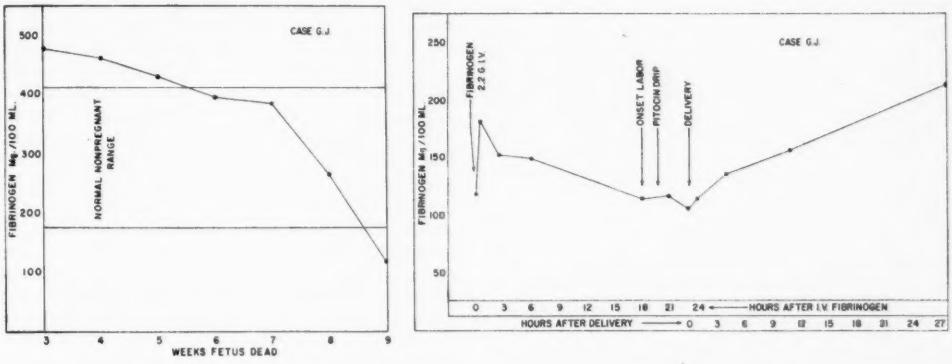


FIG. 1. Mrs. J., Case 1. a, Shown are the progressive reductions in plasma fibrinogen concentrations; by the ninth week following the intrauterine death of the fetus the fibrinogen level was abnormally low. b, The intravenous injection of 2.2 grams of fibrinogen without delivery was followed by a transient restoration of the fibrinogen concentration to normal; within 18 hours the level dropped to the preinjection value. The lack of effect of labor maintained with an infusion of pitocin on significantly changing the level of circulating fibrinogen is apparent. Following delivery without fibrinogen or blood therapy the fibrinogen concentration spontaneously returned to normal.

an elevation of the fibrinogen level from 131 to 227 milligrams per 100 milliliters. No other therapy was instituted during the next 48 hours and, as shown in Figure 5, the fibrinogen level progressively fell during this time to 174 milligrams per 100 milliliters. Then a dilatation and curettage of the uterus was undertaken with sodium pentothal as the anesthetic agent. After cervical dilatation and brief attempts at curettage the procedure was discontinued. No amniotic fluid, fetus, or placenta was obtained.

The next day, before rupture of the membranes or delivery of the fetus, the fibrinogen concentration had risen to 204 milligrams per 100 milliliters. Two and one-half days after the attempted dilatation and curettage a macerated fetus measuring 16 centimeters crown to heel was delivered spontaneously without excessive blood loss. Eight hours later the fibrinogen level was 213 milligrams per 100 milliliters. The next morning the fibrinogen concentration was 246 milligrams; at this time the somewhat adherent placenta was removed by use of ovum forceps and curettage. Bleeding was slight.

Seven days after the initial dilatation and curettage at the time of discharge from the hospital the plasma fibrinogen level was 233 milligrams per 100 milliliters. The fibrinogen levels are shown in Figure 4. Three months later she was admitted to another hospital with homologous serum jaundice.

CASE 5. A. K. (U.H. No. 673-977), pregnant for the fourth time with only 1 living child, was Rh negative and Rh isosensitized. Twice previously delivery had been effected by cesarean section. Fetal movement ceased at about 21 weeks' gestation. Except for the lack of fetal movement, the patient remained asymptomatic during the next 8 weeks.

At that time initial studies of the hemostatic mechanism were carried out. The concentration of fibrinogen in plasma was 86 milliliters per 100 milliliters, the clot lysis time of recalcified plasma was 2 days, the platelet count was 130,000 per cubic millimeter, and the plasma true prothrombic activity was 69 per cent. The clotting times in both plain glass and in silicone-coated tubes could not be determined accurately because of the small size of the clots formed. The hematocrit was 44.

The following day the patient was admitted to the hospital. Prior to fibrinogen therapy and abdominal hysterotomy, the plasma fibrinogen level was 69 milligrams per 100 milliliters, the platelet count was 110,000 per cubic millimeter, the clot lysis time was 3 days, the apparent prothrombic activity of plasma was 53 per cent, and the true prothrombic activity was 69 per cent. Total serum proteins were 6.9 grams per 100 milliliters and the albumin-globulin ratio was 1.9. The cephalin flocculation test was negative and the thymol turbidity was 1.7 Maclagan units.

Just prior to the administration of intrathecal anesthesia 4 grams of human fibrinogen were given intravenously in a period of 10 minutes. Five minutes later the plasma fibrinogen concentration was 136 milligrams per 100 milliliters and the clot observation test yielded a firm clot which entrapped most of the erythrocytes.

The abdominal hysterotomy proceeded without apparent excessive bleeding until closure of the incisions. At this time the patient went into shock and considerable bleeding from the vagina was noted. One thousand milliliters of blood was started along with a continuous intravenous infusion of diluted

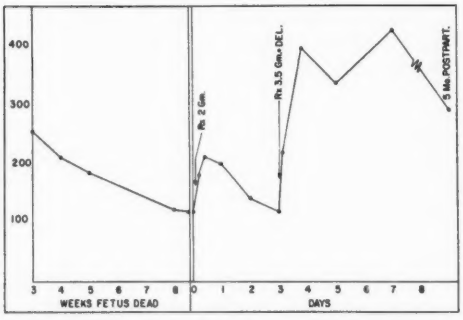


FIG. 2. Mrs. C., Case 2. Illustrated on the left are serial plasma fibrinogen levels starting 3 weeks after intrauterine death and continuing until hypofibrinogenemia was observed. To the right are shown the transient effects of injected fibrinogen without interruption of the pregnancy and then the permanent correction of the hypofibrinogenemia by injection of fibrinogen plus emptying of the uterus. The ordinate indicates fibrinogen in milligrams per 100 milliliters.

pitocin to contract the flabby, atonic uterus. This combination resulted in alleviation of the shock, a more firmly contracted uterus, and a considerable decrease in the amount of blood escaping from the vagina. Two hours after the start of the operation and at the end of 1,000 milliliters of blood, the clot observation test yielded a clot normal in size. The fibrinogen concentration at this time was 153 milligrams per 100 milliliters. Five hundred milliliters more of blood plus 1 gram of fibrinogen were then given. Shock and excessive vaginal bleeding did not recur.

Eighteen hours after delivery the plasma fibrinogen level was 190 milligrams per 100 milliliters, the apparent and true plasma prothrombic activities were 51 and 71 per cent, respectively, the clot lysis time was 3 days, and the hematocrit was 34.

The second day following delivery the patient's course was not unusual except for moderate oozing from the skin edges at the site of incision. At this time the fibrinogen level was 393 milligrams per 100 milliliters, the apparent and true plasma prothrombin activities were 60 and 93 per cent, respectively, the platelet count was 120,000, the clotting times of blood in plain glass and in silicone-coated glass tubes were normal, and the hematocrit was 33.

The bleeding from the incision spontaneously ceased and by the fourth postoperative day the fibrinogen concentration was 421 milligrams per 100 milliliters and the platelet count was 202,000 per cubic millimeter.

The patient was discharged on the tenth postoperative day at which time the fibrinogen level was 452 milligrams per 100 milliliters and the hematocrit was 33.

CASE 6. Mrs. S. (U.H. No. 617224), the subject of earlier report (5), was Rh negative and had Rh isosensitization. Intrauterine death occurred at 6 months' gestation. Eight weeks later she awoke one morning to find her mouth filled with blood. This was soon followed by extensive cutaneous ecchymoses. Thereafter the patient was observed for 4½ weeks during which time the plasma fibrinogen concentration remained remarkably constant at about 100 milligrams per 100 milliliters. The intravenous infusion of 1.05 grams of fibrinogen produced only a transient increase in the plasma concentration; within 5 hours it had returned to the preinjection level. Five grams of fibrinogen were injected intravenously just before and during a supracervical hysterectomy. Following this, the plasma concentration of fibrinogen was normal. Other studies of the hemostatic mechanism during the weeks before delivery revealed the following to be normal: platelet count, bleeding time, tourniquet test, clot retraction, clotting time in plain glass tubes, and clot lysis time. The prothrombin time was normal or slightly prolonged. The patient made an uneventful recovery.

CASE 7. Mrs. M. (U.H. No. 648020), Rh positive, pregnant for the third time and with 2 living children, last felt fetal movement at about 28 weeks' gestation. She remained asymptomatic during the next 9 weeks until the spontaneous delivery of a macerated fetus and the placenta. Moderately excessive vaginal bleeding followed delivery of the placenta. The blood pressure fell progressively to a minimum of 60/40 millimeters of mercury, 3½ hours after delivery, and an intravenous infusion of dextrose solution was begun. An hour later, before therapy with whole blood, the concentration of fibrinogen was 102 milligrams per 100 milliliters of plasma, the platelet count was 150,000 per cubic millimeter, and clotted blood lysed sometime between 3 and 7 hours. During the next 5 hours, a liter of blood was transfused intravenously. Evidences of shock promptly abated. Seven and a half hours after delivery, at a time when 500 milliliters of blood had been transfused, the concentration of fibrinogen was 123 milligrams per 100 milliliters of plasma. Twenty-four hours later it had reached 416 milligrams per 100 milliliters, the platelet count was 198,000 per cubic millimeter, and the hematocrit was 29 per cent.

CASE 8. Mrs. R. (Mt. S. No. 51766), Rh negative, delivered 5 weeks after intrauterine death which had occurred at about 28 weeks' gestation of her first pregnancy. The only symptom suggestive of abnormal hemostasis was trivial spotting of her handkerchief with blood when she blew her nose during the week before delivery, and slight bleeding from the vagina during labor. Immediately after delivery, excessive uterine bleeding began, the blood loss during the next half hour being estimated at 1,000 milliliters. Blood drawn at this time did not clot. Transfusion of compatible blood was begun. One-half hour later, a mixture of 0.9 milliliter of blood and 0.1 milligram of

topical thrombin (1,000 National Institutes of Health units per milliliter) formed a clot so small that it entrapped virtually none of the red blood cells. At the time of this clot observation test, the concentration of fibrinogen in the patient's plasma was 46 milligrams per 100 milliliters. Whole blood formed a small clot which did not lyse in 2 hours at room temperature but did dissolve in the refrigerator during the next 14 hours. Ten minutes later, an hour and a half after delivery, 4 grams of fibrinogen were injected intravenously over a period of 20 minutes. Immediately thereafter the clot observation test revealed a much larger clot and the plasma fibrinogen concentration was 149 milligrams per 100 milliliters. Therapy with fibrinogen and whole blood appeared to promptly control the hemorrhage and the patient's recovery was thereafter uncomplicated. Two days later the fibrinogen concentration was 260 milligrams per 100 milliliters.

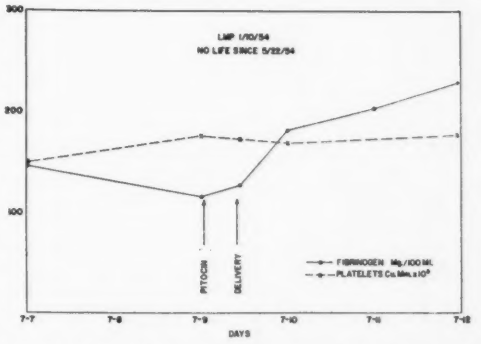


FIG. 3. Mrs. B., Case 3. Shown are the fibrinogen levels and platelet counts in a case of hypofibrinogenemia 2 days before the induction of labor with pitocin, at the start of the induction, 20 minutes after delivery, and in the postpartum period.

The concentration of fibrinogen in the plasma during labor was investigated in 12 women with intrauterine retention of a dead fetus, including 2 patients with hypofibrinogenemia. Determinations were made shortly before or very early in labor, and repeated within 1 to 20 minutes after delivery of the fetus. In 4 patients, including the 2 with hypofibrinogenemia, a continuous intravenous infusion of pitocin was given during labor. In none of the 12 patients was there a significant change in the concentration of fibrinogen in the plasma (Fig. 5).

Amniotic fluid, drawn through a No. 18 gauge needle under sterile conditions just before rupture of the membranes in Case 5, was tested for fibrinolytic activity. The fluid did not lyse bovine fibrin clots, nor did it hasten the lysis of oxalated human plasma clotted either with calcium or with thrombin.

DISCUSSION

Neither the frequency nor the pathogenesis of hypofibrinogenemia associated with prolonged intrauterine retention of a dead fetus is known. In their original report, Weiner and his associates noted that 3 of 15 Rh negative women with this syndrome developed a hemorrhagic state. In the present study, hypofibrinogenemia appeared in 8 of 31 patients. However, these data may not reflect the true incidence of abnormal hemostasis in this syndrome, since 3 of the 8 patients initially were called to our attention because they had bled. The other 5 cases were detected among a group of 28 patients first studied only because fetal death had taken place at a gestational age ranging from 12 to 36 weeks.

Although the first cases of hypofibrinogenemia with death of the fetus were in Rh negative women, it is established that the process is not peculiar to such patients. Three of the 8 patients in the present study were Rh positive.

It is apparent that the process of fibrinogen depletion need not be fulminant, as in the case of amniotic fluid embolism and in severe abruptio placentae. In at least 5 patients, hypofibrinogenemia was present for a considerable time before delivery. The patterns of fibrinogen depletion in these 5 patients were quite different from those reported recently by Hodgkinson and coworkers (2). In none of the patients with hypofibrinogenemia observed by us was there ever any evidence of spontaneous correction of the hypofibrinogenemia prior to delivery, even though in 1 patient (Case 6) hypofibrinogenemia was known to be present for at least 4½ weeks, and in 2 others (Cases 1 and 2) the concentrations of fibrinogen progressively declined over a

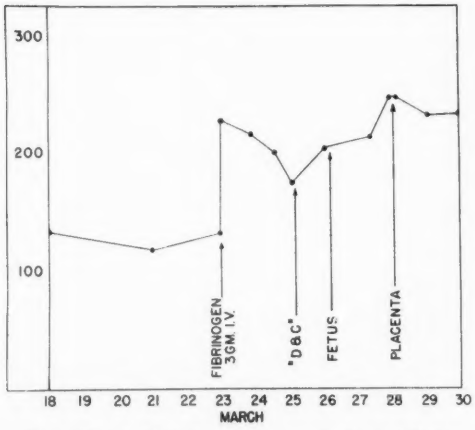


FIG. 4. Case 4. Plotted are the concentrations of fibrinogen in milligrams per 100 milliliters of plasma. Following the intravenous injection of fibrinogen there was a progressive fall toward the preinjection level until uterine dilatation and curettage was attempted. Even though none of the products of conception were removed, this surgical procedure was followed by a moderate increase in the plasma fibrinogen concentration.

period of several weeks until they reached a potentially dangerous level. Hodgkinson's group reported increases in 3 instances from a low of about 110 milligrams when first studied to reach subsequently as high as 375 milligrams of fibrinogen per 100 milliliters even though intrauterine retention of the dead fetus continued.

A further difference was noted regarding the rate of correction of the hypofibrinogenemia following delivery. They state that, although fibrinogen recovery began with evacuation of the uterine contents, unusually low values persisted for several weeks after delivery. This was not the experience in any of the present 8 cases; instead, a normal or even elevated fibrinogen level was invariably present within 48 hours after delivery.

The hypothesis that fibrinogen is destroyed by intense intravascular fibrinolytic activity is not supported by the data obtained from studies of these patients. In none was the plasma fibrinolytic activity greater than that seen in other conditions in which no fibrinogen depletion was present. Certainly in Cases 1, 2, and 6, where plasma fibrinolytic activity was normal, the apparently rapid destruction of injected fibrinogen prior to interruption of the pregnancy cannot be accounted for by this hypothesis. The frequent absence of abnormal fibrinolytic activity in the presence of hypofibrinogenemia makes it apparent that an estimation of fibrinolytic activity may be of little value for determining the presence of hypofibrinogenemia.

The explanation advanced by Weiner and co-workers that fibrinogen is consumed by intravascular coagulation, perhaps induced by thromboplastic material from the degenerating and necrotic products of conception, is more plausible. No evidence has been offered that fibrinogen production by the liver is impaired. For example, liver function tests were normal prior to delivery in Cases 1 through 6. However, the present observations indicate that any release of thromboplastic material from the products of conception must at times occur over a long period and at times at a quite constant rate rather than as a sudden overwhelming event.

One hypothesis, advanced by Vecchietti, has been that the amniotic fluid surrounding the dead fetus is fibrinolytic. However, Hodgkinson, Margulis and Luzadre (3) were unable to confirm this. Amniotic fluid obtained in Case 5 of the present series was neither directly fibrinolytic nor did it act as an activator of the fibrinolytic properties of normal plasma.

In the 7 patients with hypofibrinogenemia in whom platelet counts were made, marked thrombocytopenia was not detected. In several instances, however, the platelet concentrations were depressed below the levels found in this laboratory in normal pregnant and nonpregnant individuals (5). Moreover, marked hypoprothrombinemia was not detected when studied in 5 patients with hypofibrinogenemia but both the apparent and true plasma prothrombic activity tended to be somewhat depressed. In no instance was the moderate hyperprothrom-

binemia usually associated with normal pregnancy discovered. The mechanism of the thrombocytopenia and hypoprothrombinemia is not understood but their presence is compatible with the concept that the hypofibrinogenemia is due to intravascular coagulation.

The management of a patient with a retained dead fetus should begin as soon as the diagnosis is made. The patient should be instructed to report any hemorrhagic symptoms, however trivial. Moreover, beginning about the third week after apparent fetal death, the concentration of fibrinogen in plasma should be determined at weekly intervals. This will allow a margin of safety, since hypofibrinogenemia has not been described earlier than the fifth week after fetal death. Should the concentration of fibrinogen fall below 150 milligrams per 100 milliliters, the uterus should be emptied promptly. At least 4 grams of human fibrinogen and several units of compatible whole blood should be immediately available.

Unless there are obstetric contraindications it would appear safe to attempt induction of labor, as was done in Case 3. The data which have been described in the present study suggest that labor and vaginal delivery, with or without pitocin stimulation, will not result in any significant change in the concentration of circulating fibrinogen even if hypofibrinogenemia is present. If the induction of labor is judged not feasible or if attempts at induction fail, as they did in Case 2, abdominal hysterotomy should be carried out.

In those cases in which the induction of labor is successful, it is probably safest to give fibrinogen prior to the anticipated time of delivery. Certainly if any significant bleeding occurs during labor either from the genital tract or elsewhere, promptly 3 to 4 grams of fibrinogen should be given intravenously. It should be pointed out, however, that in 2 of the patients with hypofibrinogenemia who delivered vaginally, fibrinogen therapy was purposely withheld under carefully controlled conditions and in neither case was hemorrhage encountered, but in neither instance were there lacerations of the genital tract, episiotomies, or postpartum uterine atony. Undoubtedly, as pointed out by Barnes, a well contracted myometrium plays a major role in effecting hemostasis at the site of placental implantation immediately postpartum even in the presence of blood coagulation defects, but lacerated vessels in other parts of the genital tract do not have a vasoconstrictive mechanism comparable to the contracting myometrium.

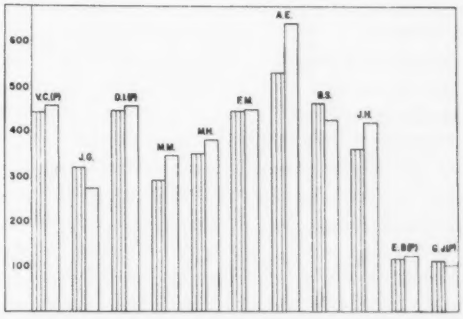


FIG. 5. Plotted are the concentrations of plasma fibrinogen before or very early in labor (ruled bar) adjacent to the concentrations 1 to 20 minutes after delivery (plain bar) in 11 cases of intrauterine death associated with delayed delivery. Hypofibrinogenemia was absent in 9 and present in 2. *P* indicates the administration of an intravenous infusion of dilute pitocin during labor.

Abdominal surgery should be performed only after giving 3 to 4 grams of fibrinogen intravenously immediately prior to surgery and in addition beginning an intravenous infusion of dextrose or saline running through a well placed 18 gauge needle. Following the emptying of the uterus close attention should be given to blood loss from the vagina. An intravenous infusion of diluted pitocin for several hours after hysterotomy is desirable to aid in the maintenance of a well contracted myometrium. If vaginal bleeding does result, the adequacy of the concentration of circulating fibrinogen should be estimated by the clot observation test described later. If a firm clot does not form in several seconds, 3 to 4 grams more of fibrinogen should be given intravenously

along with blood to combat shock. In our experience, the initial injection of fibrinogen followed promptly by the emptying of the uterus has been sufficient therapy to insure a fibrinogen level adequate for effective hemostasis in the postpartum period.

During labor and in the immediate postpartum period the following program has proved useful. The delivery room should be equipped with pyrex glass clotting tubes, either 10 by 75 or 13 by 100 millimeters in size. Some of these tubes should be scored at the 1 milliliter mark and 0.1 milliliter (2 drops) of bovine thrombin solution (1,000 National Institutes of Health units per milliliter) added to the scored tubes for use in the clot observation test. The thrombin tubes should be kept in a deep freeze readily accessible to the delivery room. Also available should be bottles or tubes containing dried oxalate salts; the ordinary blood count tube is adequate.

When hypofibrinogenemia is suspected, about 10 milliliters of blood should be drawn, preferably through a No. 18 gauge needle. Care should be exercised to avoid clotting within the syringe. The thrombin tube should be filled to the 1 milliliter mark, about 3 milliliters of blood should be transferred to an empty glass tube, and 5 milliliters should be oxalated. Normally, a firm clot will appear within a few seconds in the thrombin tube. In the presence of hypofibrinogenemia, the clot may at first appear normal, but if the tube is tapped gently, the clot will retract to a small ball from which most of the red cells will be extruded. This clot observation test, first suggested in this connotation by Page, gives an almost instant result and is therefore most useful. As an additional check, the 3 milliliters of blood in the glass tube should also be observed at frequent intervals to see if clotting takes place and if the clot which forms is abnormally flabby or retracts to a small nubbin, suggesting hypofibrinogenemia. Failure of blood to clot in both the thrombin and plain tubes indicates the presence of afibrinogenemia. In spite of reports to the contrary, clotting times have been of little value in our experience in diagnosing hypofibrinogenemia since normal clotting times may be observed despite severe hypofibrinogenemia. The oxalated blood properly treated and stored may be used for the quantitative determination of fibrinogen, but usually a therapeutic decision must be made before the result of this test is available.

If hypofibrinogenemia or afibrinogenemia is detected 4 grams of human fibrinogen should be injected intravenously along with compatible whole blood to combat shock. If the fetus is undelivered, steps should be taken to empty the uterus while the patient's plasma fibrinogen is maintained at a normal level, as indicated by the clot observation test. The evidence at present indicates that once the uterus is emptied the process of apparent defibrination ceases and hemostasis can be maintained without further administration of fibrinogen. If human fibrinogen is not available, whole blood should be used as a source of fibrinogen. This was successful in Case 5, but others have reported that under some circumstances the administration of blood alone was not adequate in restoring the patient's plasma fibrinogen level, and human fibrinogen would appear to be the agent of choice.

SUMMARY

1. The concentration of fibrinogen in the circulating blood has been determined at or near the time of parturition in 31 women with intrauterine retention of a fetus dead for a period of 3 to 12 weeks prior to delivery.

2. In these patients, hypofibrinogenemia was detected in 5 patients prior to delivery, at a time when no hemorrhagic manifestations were noted. In another, hypofibrinogenemia was observed prior to delivery, at a time when bleeding manifestations were evident. In 2 others, hypofibrinogenemia was noted after hemorrhage immediately postpartum.

3. Serial studies indicate that the process of fibrinogen depletion may be slowly progressive rather than fulminating, and that labor and vaginal delivery per se, even with pitocin stimulation, need not be deleterious to the patients' hemostatic mechanisms.

4. A method of management for the patient with prolonged intrauterine retention of a dead fetus is outlined.

REFERENCES

1. Barnes, A. C. Postpartum blood; its clotting mechanism and relationship to the peripheral blood picture. Am. J. M. Sc., 1947, 213: 463.
2. Hodgkinson, C. P., Luzadre, J. H., Pifer, P. W., Swinehart, L. A., and Remp, D. G. Hypofibrinogenemia and defects of coagulation. Obst. Gyn., 1955, 5: 465.
3. Hodgkinson, C. P., Margulis, R. R., and Luzadre, J. H. Etiology and management of hypofibrinogenemia of pregnancy. J. Am. M. Ass., 1954, 154: 557.
4. Page, E. W. In discussion of Kellogg, F. S. Hemorrhagic tendencies in toxemia of pregnancy. Obst. Gyn. Survey, 1948, 3: 746.
5. Ratnoff, O. D., Colopy, J. E., and Pritchard, J. A. The blood-clotting mechanism during normal parturition. J. Laborat. Clin. M., 1954, 44: 408.
6. Ratnoff, O. D., Lauster, C. F., Sholl, J. B., and Schilling, M. O. A hemorrhagic state during pregnancy with the presence of maternal Rh antibodies, death of the fetus and hypofibrinogenemia. Am. J. Med., 1952, 13: 111.
7. Ratnoff, O. D., Pritchard, J. A., and Colopy, J. E. Hemorrhagic states during pregnancy. N. England J. M., 1955, 253: 63.
8. Vecchietti, G. Contributo allo studio delle emorragie post-partum per afibrinogenemia. Rev. obst. gin., Caracas, 1953, 8: 443.
9. Weiner, A. E., Reid, D. E., Roby, C. C., and Diamond, L. K. Coagulation defects with intrauterine death from Rh isosensitization. Am. J. Obst. Gyn., 1950, 60: 1015.

PHYSIOLOGIC ALTERATIONS WITH MASSIVE BLOOD REPLACEMENT

WILLIAM S. HOWLAND, M.D., OLGA SCHWEIZER, M.D.,
C. PAUL BOYAN, M.D., and ALMA C. DOTTO, M.D., New York, New York

THE FACT THAT DELETERIOUS EFFECTS may result from the use of large quantities of blood prepared with citrate has been known for several years. In 1943 Ivy and his co-workers working with dogs demonstrated the inferiority of citrated blood to that prepared with gelatin, heparin, or a process of defibrination in producing a blood pressure response after severe hemorrhage. Their results were confirmed by Bruneau and Graham who showed that the survival rate in dogs subjected to repeated bleeding was shorter when citrated blood was employed as a replacement in comparison with the heparinized variety. When Cookson and his co-workers bled dogs to 50 per cent of their calculated blood volume and replaced the loss with heparinized blood within 5 to 10 minutes, they were able to effect a restoration of blood pressure in every animal. The use of citrated blood not only produced a negligible vasopressor response in 60 per cent of the dogs but also resulted in cardiac depression.

Other experimental work by Nakasone and associates has demonstrated that the rapidity of injection of citrated blood is an important factor in producing alterations in blood pressure and a rapid terminal collapse.

METABOLISM OF CITRATE

The plasma of normal healthy human subjects contains approximately 3 milligrams of citrate per 100 cubic centimeters, estimated as citric acid. Citrate, introduced into the blood stream, is rapidly metabolized by the liver. Mallinson has shown that isolated livers of animals infused with a hundred times the normal concentration of plasma citrate effected an almost complete clearance of the citrate after a single passage of the perfusate. In the presence of hepatic disease there is both a higher level of plasma citrate and a decreased rate of liver clearance.

From the Division of Anesthesiology, Memorial Center for Cancer and Allied Diseases and Sloan-Kettering Division, Cornell University Medical College, New York.

SOURCE OF MATERIAL

With the advent of radical surgical procedures for the treatment of cancer, the physiologic effects of massive blood transfusion have become a matter of prime consideration. For the purpose of this review massive blood transfusion is defined as the administration of 5,000 cubic centimeters or more of blood, an amount equal to the total blood volume in an average adult male.

The material studied includes 130 consecutive patients who received 10 or more citrated transfusions during the course of operation and a second series of 123 patients to whom 5 to 9 pints of blood were administered. Preoperative and postoperative transfusions are not included in the total number.

The patients in this series, who varied in age from 23 to 79 years, were subjected to radical surgical procedures for cancer in various anatomic regions. The type and case distribution of anesthetic agents are summarized in Table I. Standard anesthetic techniques were employed throughout both groups.

RESULTS

An analysis of the 253 cases in the present series indicates that the physiologic derangements encountered in patients who receive

massive blood replacement fall into two general categories: (1) a hemorrhagic diathesis or failure of the clotting mechanism and (2) a cessation of cardiac function (either ventricular fibrillation or primary asystole). Fifty-six or 43 per cent of the 130 patients to whom 5,000 cubic centimeters or more of blood were administered developed one or the other of these major complications.

TABLE I.—SUMMARY OF MATERIAL STUDIED

	5–9 transfusions No.	*10 or more transfusions* No.
Total No. of patients	123	130
Age, years		
20–29	7	5
30–39	5	11
40–49	30	32
50–59	46	56
60–69	30	18
70 and over	5	8
Anatomic regions involved in operation		
Head and neck	30	17
Pelvis	53	88
Upper abdomen	23	10
Liver	1	8
Chest	11	5
Extremity	5	2
Anesthetic agent		
Thiopental	24	17
Ether	71	83
Cyclopropane	23	29
Spinal	5	1

HEMORRHAGIC DIATHESIS

It is apparent that the development of a hemorrhagic diathesis depends largely on the volume of blood replacement since all but 3 of these cases occurred after transfusion of 10 pints of citrated blood and the majority after 12 pints. Rapidity of transfusion characterized the 3 cases that developed oozing after smaller amounts of blood, 2 after 7 pints and 1 after 8. Since failure of the clotting mechanism was not an important factor in the 22 cases of cardiac arrest, the statistics presented in Table II are based on the 108 individuals who survived the operative procedure. From these tables it can be seen that approximately one-third of all patients receiving 10 or more pints of blood developed a hemorrhagic diathesis before the termination of surgery. Except for the probably greater incidence, 45 per cent, of this complication in patients anesthetized with cyclopropane, the type of anesthetic agent appeared to play an insignificant role. Age was not an important factor in the development of an abnormal bleeding tendency.

CESSATION OF CARDIAC FUNCTION

The second major physiologic derangement associated with massive blood transfusion is a sudden cessation of cardiac function which occurred in spite of adequate replacement of the blood lost during the operative procedure. In 9 of the 22 cases of this condition changes were demonstrated in the electrocardiogram diagnostic of ventricular fibrillation and 2 were cases of cardiac asystole without fibrillation. Unfortunately electrocardiographic tracings were not available in the remaining patients in this group. In addition to the 22 patients who died after receiving 10 or more pints of blood there were 3 additional deaths in the series transfused with 5 to 9 pints. The type of surgical procedure associated with this mortality is illustrated in Table III. The high incidence of fatality in resection of the liver is significant in view of the fact that the liver represents the main site of citrate metabolism.

In contrast to the development of a hemorrhagic diathesis, in which the total volume of blood replacement rather than the rapidity of transfusion seemed to play the major precipitating role, the appearance of cardiac malfunction paralleled the speed of administration of the blood. Seventy-five per cent of the patients in this group demonstrated asystole or ventricular fibrillation during the first 2 hours of the operative procedure as a sequel of receiving large volumes of blood within a relatively short period of time and several deaths occurred during the first hour.

The role of the anesthetic agent in the production of this complication is not clearly defined but, from the statistics presented in Table III, it appears that cyclopropane may play more than a passive role. In the

TABLE II.—HEMORRHAGIC DIATHESIS IN 108 PATIENTS WHO SURVIVED OPERATION

	10 or more transfusions	
	No.	*Per cent*
Anatomic regions involved in operation		
Head and neck	6 of 17	35.3
Pelvis	26 of 74	35.1
Upper abdomen	2 of 10	20.0
Liver	1 of 2	50.0
Chest	1 of 3	33.3
Extremity	none of 2	0.0
Anesthetic agent		
Thiopental	5 of 17	29.4
Ether	22 of 70	31.4
Cyclopropane	9 of 20	45.0
Spinal	none of 1	0.0

group receiving 10 or more pints of blood death occurred in 9 of 29 patients (31 per cent) anesthetized with cyclopropane in contrast to 13 of 83 (15.6 per cent) who received ether. Cyclopropane was administered to all 3 fatalities in the series transfused with 5 to 9 pints.

It is evident from Table III that the age of the patient was a matter of no importance.

DISCUSSION

Before proceeding with a more detailed discussion of this subject, it should be noted that Weiner found that replacement therapy equivalent to 1 blood volume results in the presence of 62 per cent of donor blood in the patient's circulation. The administration of 2 blood volumes (approximately 20 pints) leaves the individual with only 13 per cent of his original blood, 87 per cent having been introduced into his circulation from an outside source.

These figures assume added significance in view of the fact that all patients in the present series who received more than 18 pints of citrated blood developed either a hemorrhagic diathesis or some form of cardiac malfunction. Although it seems obvious that the occurrence of these complications is directly related to the number of units of blood replacement and, in the latter case especially, to the rapidity of transfusion, the exact factors responsible for these untoward results are still a subject of discussion.

In recent years the theories advanced to explain the mechanism of blood coagulation have become increasingly complicated and the hemorrhagic tendency may be attributable to one or more of the several phases of this process.

According to Stefanini platelets have assumed an increasingly significant role in the process of hemostasis and blood coagulation since they supply agents active in every phase of the clotting process. Included among these agents are a vasoconstrictor substance (serotonin), a second agent indispensable for activation of thromboplastin, and a third that determines retraction of the clot. It is a well known fact that stored bank blood has a marked deficiency in platelets. Although the human body is capable of the replacement of these platelets lost during hemorrhage the new young platelets may be deficient in the various factors concerned with blood coagulation.

Recently, Bunker and his co-workers have measured citric acid levels after multiple blood transfusions. They found that normal adult patients who received several transfusions at a rate of not more than 500 cubic centimeters every 30 minutes gave no evidence of citric acid intoxication. However, patients with liver disease showed elevated serum citrate levels with relatively small amounts of blood. Concomitantly they found a reduction in the level of ionized calcium in the serum of many of their patients. They suggest that calcium chloride may be given intravenously but stressed the danger of calcium overdose with possible deleterious effects on the myocardium. In the present series abnormal bleeding developed in spite of the prophylactic administration of 1 gram of calcium gluconate for every 1,000 cubic centimeters of blood, but the degree of ionization of this compound may not have provided adequate replacement of the calcium bound by citrate.

During the course of their studies on casualties of the Korean War, Scott and Crosby noted a tendency toward a hemorrhagic diathesis in patients who had received over

20 pints of blood within a short time. Further investigation revealed a normal clotting time with a 50 per cent reduction in prothrombin activity in men transfused with 4,500 cubic centimeters or more of blood. Although they believed that this deficiency in prothrombin was probably due to lack of the labile factor, addition of this factor did not result in a restitution of normal prothrombin activity in every case. In comparing Scott's studies with the ones reported in this review it must be remembered that Korean War army casualties were largely healthy young men prior to injury whereas the subjects in the present series were patients with advanced cancer many of whom had been subjected to previous operative procedures.

A final mechanism suggested for the development of abnormal bleeding after massive transfusion is the process of fibrinolysis. Anoxia is believed to catalyze clot destruction. Although the patients in the present series were clinically well oxygenated, fibrinolysin titers were not obtained so that it is impossible to offer any further discussion of this topic.

The exact mechanism by which rapid transfusion of large quantities of citrated blood produces either cardiac standstill or ventricular fibrillation is still in doubt but a review of the action of various ions on the heart leads to the conclusion that an excess of one or more of these components of preserved blood may result in cessation of cardiac action.

Stewart and his co-workers have shown that hyperkalemia results in interventricular block and cardiac arrest in diastole. Crosby reported plasma potassium levels as high as 15 milliequivalents per liter after storage of bank blood for 12 to 15 days and the majority of blood banks will not employ blood after the twentieth day since at that stage plasma potassium may reach a level of 20 milliequivalents per liter. The relatively high mortality in the present series associated with cyclopropane anesthesia could be explained on the basis of increased myocardial irritability resulting from a combination of hyperkalemia and the action of the anesthetic agent.

TABLE III.—DEATHS IN OPERATING ROOM

	5-9 transfusions		*10 or more transfusions*	
	No.	*Per cent*	*No.*	*Per cent*
Anatomic regions involved in operation				
Pelvis	3 of 53	5.7	14 of 88	15.9
Liver			6 of 8	75.0
Chest			2 of 5	40.0
Head and neck, upper abdomen, extremity	0		0	
Anesthetic agent				
Ether	0		13 of 83	15.6
Cyclopropane	3 of 23	13.0	9 of 29	31.0
Thiopental	0		0	
Spinal	0		0	
Age, years				
20–29	0		1 of 5	20.0
30–39	0		1 of 11	9.0
40–49	1 of 30	3.3	6 of 32	19.0
50–59	1 of 46	2.1	9 of 56	16.0
60–69	1 of 30	3.3	4 of 18	22.0
70 and over	0		1 of 8	12.5
Total	3 of 106	2.8	22 of 130	16.9

The toxic effects of excess citrate have been known for several years. Cookson theorized that the deleterious results produced by citrate are due to removal of ionized calcium with resultant impairment of myocardial contraction and cardiac standstill in diastole. In corroboration of this hypothesis Watkins found that the untoward effects of the rapid administration of large amounts of citrate could be counteracted by the administration of calcium gluconate or calcium chloride. In the present series on several occasions changes in the electrocardiogram suggestive of impending cardiac difficulties were improved by an increase in the dosage of calcium gluconate. Although this is suggestive evidence that citrate intoxication or hyperkalemia may play an important role in the production of cardiac malfunction after massive transfusion, sufficient laboratory evidence has not been obtained up to the present time to justify a more definite statement.

Marked cooling of the viscera is a fact observed by many surgeons after massive blood replacement and is usually premonitory of impending diaster. This is significant

inasmuch as Deterling and his co-workers found that about one-third of all dogs subjected to experimental hypothermia developed ventricular fibrillation. There was a direct correlation between the degree of cooling and the onset of ventricular hyperirritability. Cookson also found that hypothermia enhanced the effects of citrate intoxication.

It is thus obvious that many factors, either alone or in combination, may predispose to cardiac malfunction in patients receiving rapid transfusion of citrated blood.

SUMMARY AND CONCLUSION

1. The physiologic effects of massive blood transfusion fall into two main categories: hemorrhagic diathesis and cardiac malfunction in the form of asystole or ventricular fibrillation.

2. The possible causative factors have been reviewed.

3. It seems probable that citrate intoxication may play an important role in the development of cardiac asystole and ventricular fibrillation.

REFERENCES

1. Bruneau, J., and Graham, E. A. The caution against too liberal use of citrated blood in transfusions. Arch. Surg., 1943, 47: 319–325.
2. Bunker, J. P., Stetson, J. B., Coe, R. C., Grillo, H. G., and Murphy, A. J. Citric acid intoxication. J. Am. M. Ass., 1955, 157: 1361–1367.
3. Cookson, B. A., Costan-Durieux, J., and Bailey, C. P. The toxic effects of citrated blood and the search for a suitable substitute for use in cardiac surgery. Ann. Surg., 1954, 139: 430–438.
4. Crosby, W. H. Personal communication.
5. Deterling, R. A., Nelson, E., Bhonslay, S., and Howland, W. S. A study of basic physiologic changes associated with hypothermia. Arch. Surg., 1955, 70: 87–94.
6. Ivy, A. C., Greengard, H., Epstein, I., Grodins, and Dutton, D. F. The effects of various blood substitutes in resuscitation after an otherwise total hemorrhage. Surg. Gyn. Obst., 1943, 76: 85–90.
7. Mallison, P. L. Blood Transfusion in Clinical Medicine. Blackwell, Oxford: Scientific Publication Limited, 1951.
8. Nakasone, N., Watkins, E., Janeway, C. A., and Gross, R. E. Experimental studies of circulatory derangement following the massive transfusion of citrated blood. J. Laborat. Clin. M., 1954, 43: 184–195.
9. Scott, R., and Crosby, W. H. Changes in coagulation mechanism following wounding and resuscitation with stored blood; a study of battle casualties in Korea. Blood, N. Y., 1954, 9: 6: 609–621.
10. Stefanini, M. Mechanism of blood coagulation in normal and pathologic conditions. Am. J. Med., 1953, 14: 64–86.
11. Stewart, H. J., Shepard, E. M., and Harger, E. L. The electrocardiographic manifestations of potassium intoxication. Am. J. Med., 1948, 5: 821–827.
12. Watkins, E., Jr. Experimental citrate intoxication during massive blood transfusion. Surgical Forum 1953; American College of Surgeons. Pp. 213-219. Philadelphia and London: W. B. Saunders Co., 1954.
13. Weiner, A. S., and Wexler, J. B. The use of heparin when performing exchange blood transfusions in newborn infants. J. Laborat. Clin. M., 1946, 31: 1016–1019.

MORBIDITY OF ABDOMINOPERINEAL RESECTION

JOSEPH A. BUCKWALTER, M.D., F.A.C.S., Iowa City, Iowa, RICHARD SHROPSHIRE, M.D., Great Falls, Montana, and BENNETT A. JOINER, M.D., F.A.C.S., San Angelo, Texas

AT THE BEGINNING of the present century, Miles began to practice and later described a technique which he had developed for the radical excision of rectal carcinomas through a combined abdominoperineal approach, an operation first done by Czerny in 1884. The basic principle embodied has proved sound and remains the basis today for treatment of this lesion.

The criteria of operability, technical considerations, operative mortality, and the results achieved by surgical therapy have quite correctly concerned surgeons who are interested in this problem. Although the operation is recognized as one of considerable magnitude attended by very real postoperative morbidity, surprisingly little attention has been directed to the study of the postoperative complications. General discussions have been included in the monographs and the many papers which deal primarily with other aspects of the surgical treatment of distal colon and rectal lesions. Few studies concern themselves specifically with the general complications, although considerable attention has been directed to the urologic complications which are made conspicuous by their high incidence.

PURPOSE OF STUDY

Our objective was to study the various complications occurring in patients upon whom combined abdominoperineal resection had been done. This information will help point out shortcomings of our present methods and suggest changes which will, it is hoped, result in lowered morbidity and mortality. This study likewise will provide a baseline useful in assessing the value of technical changes which may be made in the performance of this operation at the University of Iowa Hospitals.

In this article we will describe and report the observed postoperative complications in this series of patients. Possible relationships between preoperative and operative factors, and the observed morbidities will be discussed in a second paper now in preparation.

MATERIAL

The clinical data were obtained from the case histories of 176 unselected patients upon whom a combined abdominoperineal resection was performed during the 5 year period, 1947 to 1951 (Table I). Differences in regard to preoperative preparation, indications for surgery, the type of anesthesia, and postoperative care were minor.

During the preoperative period, which averaged 7.2 days, a high protein, high vitamin, and low residue diet was given; the bowel was cleansed with sulfasuxidine and saline cathartics. Indicated measures were carried out to correct blood volume and nutritional, cardiovascular, and urinary tract deficiencies. The operation performed was basically as described by Miles. All procedures were performed by one surgeon, either a member of the staff or a resident under his supervision. The synchronous two team approach was not employed. Those patients in whom pelvic exenteration was done were not included. The average postoperative stay was 21.9 days excluding postoperative deaths. Gastric suction was discontinued and diet started as permitted by the patient's progress. Supportive and specific therapeutic measures were used as indicated.

Of the 176 patients, 111 had complications; 65 had no complications. The average

From the Department of Surgery, College of Medicine, State University of Iowa, Iowa City, Iowa.

TABLE I.—CLINICAL DATA ON 176 PATIENTS

Diagnosis	*No. of patients* — *Male*	*Female*	*Total*	*Age of patients, years* — *Range*	*Average*
Adenocarcinoma of the rectum without extension..	57	26	83	18–84	66.0
with extension....	27	26	53	31–81	65.5
Total.....	84	52	136	18–84	65.8
Epidermoid carcinoma of the anus or rectum.....	5	5	10	46–70	58.5
Ulcerative colitis.....	5	11	16	18–59	36.5
Multiple polyposis.....	1	3	4	20–41	32.5
Premalignant rectal polyp.	1	2	3	52–68	60.5
Others.....	0	7	7	50–66	59.5
Totals.....	96	80	176	18–84	62.0

postoperative stay was 21.9 days, 26.5 days for those with complications and 15.7 for those without complications. Complications were divided into those occurring during the period of postoperative hospitalization designated as early and those developing following discharge designated as late. The early complications have been subdivided into nonurologic and urologic (Table II).

EARLY NONUROLOGIC COMPLICATIONS

In Table III is listed the number of times each complication was encountered. Several types of abdominal wound complications were noted. Evisceration requiring closure happened 2 times; neither instance resulted in a fatality. Separation of the skin or fascia which did not require surgical intervention took place in 4 cases. In 1 patient a fatality followed when an unrecognized separation of the peritoneum resulted in the incarceration of a loop of small bowel, strangulation, and perforation. The remaining 16 cases of abdominal wound complications included stitch abscesses, cellulitis, and suppurative processes of varying magnitudes, some of which required surgical intervention. Of first importance in the understanding and prevention of wound complications is the nutritional state of the patient, gentleness to tissues with protection of the wound edges during surgery, proper closure with accurate approximation of the wound edges, and prevention of postoperative distention. Correct treatment consists of prompt recognition and institution of indicated measures to assure adequate drainage and control of the local or systemic process.

TABLE II.—POSTOPERATIVE COMPLICATIONS*

	No. of cases	*Percentage of patients*	*No. of complications*
Total.....	111	63	206
Early.....	92	51	166
Nonurologic	78	44	122
Urologic.....	34	19	44
Late.....	32	18	40

*Single patients many times had multiple complications—early and late, nonurologic and urologic—which fact is responsible for the apparent numerical discrepancies noted in this table.

Intragastric suction was discontinued in the average case on the third postoperative day. If there was no peristalsis and suction was required after the fifth day, or when suction had to be restarted and continued after discontinuance, the complication ileus was considered to exist. The important differentiation from mechanical obstruction was made by relying chiefly upon the clinical examination, usually supported by the findings on x-ray examination of the abdomen in the supine and upright positions. Operative manipulation of the bowel, varying degrees of peritoneal contamination, and a depleted patient were the most important causative factors. All these patients ultimately responded favorably to conservative measures and none was operated upon.

Mortalities occurring before discharge within 60 days following operation were considered to be early complications (Table IV). The operative mortality rate of 9.6 per cent is similar to that reported from other teaching centers. Substantially lower mortality rates are recorded by private practice clinics. Differences in patient population, operative indications, and operative experience of the surgeons probably caused this discrepancy.

Seven of the patients who died as a result of massive pulmonary embolization had no antemortem clinical evidence of thrombophlebitis or phlebothrombosis. This fatal complication was announced by sudden collapse with hypotension, dyspnea, cyanosis, loss of consciousness followed promptly by death in a patient who had been enjoying an uncomplicated postoperative course.

A loop of ileum became incarcerated between the colostomy and lateral peritoneal

wall in 1 patient. Strangulation, gangrene, perforation, and death followed. The same sequence of events followed the incarceration of a loop of small bowel in an unrecognized separation of the peritoneum as has already been mentioned. In a third patient reoperated upon on the seventh postoperative day, volvulus of a loop of jejunum secondary to omental adhesions was found. The patient succumbed 9 days following resection of a gangrenous segment of bowel as a result of continuing ileus, pneumonia, and renal failure. Rankin and Johnston have found mechanical obstruction more often the cause of postoperative mortality. Adequate reperitonealization of denuded areas, careful closure of wounds, proper construction of the colostomy to prevent incarceration of bowel loops, and gentle handling of peritoneal surfaces during the operation will reduce the chances that this complication will occur.

Renal failure resulting in uremia with electrolyte imbalance with excessive sodium loss was the primary cause of death in 1 patient. Rupture of an arteriosclerotic aneurysm caused the death of another patient who had had a protracted postoperative course complicated by ileus and abdominal wound infection. Fatal peritonitis occurred as a result of inadvertent contamination of the peritoneal cavity at the time of operation. The 1 patient in whom postmortem examination was not performed died suddenly on the ninth postoperative day with the typical clinical findings of pulmonary embolism.

Perineal wound complications were all inflammatory ones. Contamination at operation, postoperative bleeding, and incomplete drainage of the presacral space were the causative factors. In 3 instances operative intervention was required to secure adequate drainage. The remainder responded to removal of stitches, irrigations, and sitz baths.

Atelectasis occurred during the first 3 postoperative days in 7 patients. If deep breathing, coughing, endotracheal aspiration proved ineffectual, bronchoscopy was carried out without delay. Five patients developed pneumonia. The 1 instance of food aspiration terminated fatally. Stress was placed on early postoperative breathing exercises and the other measures mentioned.

TABLE III.—122 EARLY NONUROLOGIC COMPLICATIONS

	No. of cases	*Per cent of patients*
Abdominal wound	23	13.0
Ileus	17	9.7
Death	16	9.1
Perineal wound	14	8.0
Pulmonary	12	6.8
Thrombophlebitis	9	5.1
Gastric dilatation	8	4.5
Cardiovascular	8	4.5
Colostomy	6	3.4
Mechanical obstruction	5	2.8
Peritonitis	2	1.2
Toxic psychosis	1	0.6
Vaginal perineal fistula	1	0.6

In the patients developing thrombophlebitis, clinical signs appeared from the fourth to eighth postoperative day. All parts or segments of the iliac venous system were involved as was also true in the patients who died of pulmonary embolism. Treatment included anticoagulants, compression of the superficial veins by elastic bandages, antibiotics, and in 3 cases superficial femoral vein ligation. The 1 patient who died as the result of a massive pulmonary embolus had received anticoagulants for 48 hours before death. Including 11 additional cases in which pulmonary emboli were found at necropsy, 10.8 per cent of the entire group of patients had definite evidence of this most distressing complication.

Gastric dilatation was noted during the first postoperative week usually shortly after intragastric suction had been discontinued. Characterized by dyspnea and prostration, improvement promptly followed removal of

TABLE IV.—MORTALITIES

Principal cause of death	*No. of cases*	*Postop. day*
Massive pulmonary embolism	8	9*
Mechanical obstruction	3	13*
Electrolyte imbalance with uremia	1	7
Rupture aortic aneurysm	1	57
Peritonitis	1	16
Pneumonia	1	17
No necropsy (pulmonary embolism)	1	9
Total	16	14*

*Average

TABLE V.—44 EARLY UROLOGIC COMPLICATIONS

	No. of cases	*Percentage of patients*
Retention	30	17.0
Infection	8	4.5
Urethral perineal fistula	4	2.3
Uremia	2	1.2

the retained gastric contents. Four patients developed cardiac decompensation which responded well to the usual measures. Nonfatal coronary occlusion in 1 and disturbances in the cardiac conduction mechanism were observed in 5 patients.

Strictures of the colostomy which required revision before discharge occurred in 4 patients. Colostomies brought through a stoma separate from the wound, opened at once and sewed to the skin margin, seemed less prone to become strictured. Retraction of the colostomy requiring immediate operative intervention occurred 2 times.

In addition to the 3 fatal cases, reoperation was required in 2 additional cases of mechanical obstruction caused by an adhesion in one and incarceration of an ileal loop in a pelvic peritoneal defect in the other. An exhaustive study of this postoperative complication has been reported by Goligher and associates. One fatal and 1 nonfatal instance of peritonitis followed peritoneal contamination which occurred at the time of operation. A toxic psychosis occurring in a patient who otherwise had an uncomplicated postoperative course remains unexplained. Postoperative perineal wound infection, coupled with an extensive perineal dissection required to remove a huge low-lying neoplasm, resulted in a vaginal perineal fistula which ultimately closed.

About 15 per cent of the patients had postoperative hypotensive episodes which responded to the administration of blood suggesting incomplete replacement of the blood lost during the operation. No massive bleeding occurred during the postoperative period. Temperature elevation was considered a sign of, rather than, a complication as was borne out by the fact that the 71 patients with elevations all developed at least 1 early complication.

EARLY UROLOGIC COMPLICATIONS

Table V shows the incidence of these complications. In the average patient, catheterization was not required after the twelfth postoperative day. Usually the Foley catheter was first removed on the seventh postoperative day. Most patients were unable immediately to empty the bladder completely. This tendency for retention usually responded satisfactorily to intermittent catheterization, or several additional days of the indwelling catheter. The complication retention was considered to exist when by the twenty-first postoperative day the patient continued to have a residual urine volume in excess of 125 to 150 cubic centimeters on being catheterized immediately following voiding.

Rather than a single cause, it seems most likely that there are multiple ones responsible for retention in each case which vary in their importance from 1 patient to another. Cystometric studies in these patients revealed that very rarely was there evidence of a disturbance in innervation or function of the detrussor muscle thus agreeing with the findings of Coller and Eastman. Since the parasympathetic innervation is derived from sacral roots in 2, 3, and 4 there should be little chance for injury to the bladder innervation providing the usual planes of dissection are adhered to. Additional evidence is provided by the observation that retention occurred in the same incidence in a group of patients upon whom posterior resection was performed without pelvic dissection from above as in a similar group of patients undergoing a Miles type abdominoperineal resection reported by Marshall and associates. When, because of the size and character of the lesion, it was necessary to strip the presacral fascia, the neurogenic type of bladder frequently resulted.

Incident to the perineal dissection, the support for the urogenital diaphragm and external uretheral sphincter is disturbed to a greater or lesser degree. When extensive anterior dissection has been necessary, pos-

terior tilt of the bladder may occur and be accompanied by angulation of the bladder neck and of the urethra. This results in mechanical interference with normal micturition. Disturbance of the normal anatomic relations may result in a disturbance of function of the external urethral sphincter, thus adding to the retention. Infection almost inevitably accompanies the use of an indwelling or intermittent catheter. With the advent of urinary antiseptics, better control of this factor has become possible. However, there were several patients in whom this appeared to be the most important factor. Incipient preoperative prostatism was accompanied almost invariably by postoperative retention.

Transurethral resection was done in 4 cases of postoperative urinary retention. This procedure was reserved for the patient with the definitely enlarged obstructing prostate or the patient who continued to have retention 2 or 3 months following operation. Most patients responded to prolonged indwelling or intermittent catheterization, control of the infection by urinary antiseptics, and careful attention to the technique of catheter use. This suggests that an important role is played by the stabilization of the bladder, urogenital diaphragm, and urethra which occurs as healing progresses in the pelvis and perineum. Of interest in this regard is the case report of a patient with protracted postoperative retention who had normal bladder function following operative resuspension of the bladder described by Marshall and associates.

Infections, as a primary complication, occurred without urinary retention. Four patients had hemorrhagic purulent cystitis which responded to continued catheter drainage and urinary antiseptics. Ascending urinary tract infection resulting in pyelonephritis happened 2 times. A suprapubic cystostomy was required to help control a severe urethritis which occurred 10 days following operation in 1 case. Another patient first developed urethritis; prostatis, epididymitis, and orchitis followed.

TABLE VI.—40 LATE POSTOPERATIVE COMPLICATIONS

	No. of cases	*Percentage of patients*
Colostomy strictures	20	11.4
Perineal wound	7	4.0
Colostomy hernia	4	2.3
Abdominal wound	3	1.7
Ileus	2	1.2
Mechanical obstruction	2	1.2
Urethral stricture	2	1.2

Urethral perineal fistula resulted from continuing perineal wound infection following injury to the urethra incident to necessarily radical perineal dissection of large anteriorly placed lesions. With replacement of the catheter and control of the persisting perineal infection, the fistulas closed; late urethral strictures occurred in 2 of these cases. Continuing renal insufficiency with uremia resulted in one operative mortality; the other patient died as a result of renal failure several months following discharge.

LATE COMPLICATIONS

In Table VI are tabulated the complications which developed following the patients' discharge. Follow-up data were obtained relative to 130 patients a year or later after operation. Since data relative to late complications were incomplete, the number which occurred was probably larger than that here reported.

Stricture occurred in 11 instances in which the colostomy had been brought through the wound and in 9 patients in whom it had been brought through a separate wound. Most often low grade infection around the colostomy followed by healing with contraction of the scar resulted in constriction at the junction with the skin and subcutaneous tissue. Continuing digital dilatation resulted in a satisfactorily functioning colostomy in 13 of the patients. Marked narrowing producing obstruction, or a failure to respond to dilatation, resulted in operative revision in 7 instances. No strictures following revision have been noted.

Three months after operation, drainage caused by persisting low grade infection continued from 7 perineal wounds. In all cases

the cause was inadequate drainage of postoperative presacral fluid collections. Accurate hemostasis, absence of contamination and early recognition with adequate drainage of such collections during the immediate postoperative period will obviate this complication. Late surgical incision and drainage were required in 3 instances. Daily irrigation or sitz baths resulted in cessation of the discharge and healing of the wound in the remaining patients.

All 4 colostomy hernias occurred in patients in whom the colostomy had been brought through the wound. A common denominator was the presence of infection in the wound adjacent to the colostomy following operation. Similarly, infection was the common denominator in the 3 cases of postoperative abdominal wound hernia. All 7 hernias were repaired.

The cause for the ileus which occurred late in 2 patients was not detected. Reoperation was done upon the 2 patients who developed late mechanical obstruction. In one it was necessary to resect a strangulated loop of ileum which had become incarcerated between the colostomy and the lateral peritoneal wall. The lateral gutter had not been closed in this patient. Obstruction was relieved by lysis of an adhesive band in the other patient.

SUMMARY

The postoperative complications which followed the Miles type combined abdominoperineal resection performed consecutively upon an unselected group of 176 patients during the years 1947 through 1951 at the University of Iowa Hospitals have been reported. Sixty-three per cent of the patients developed one or more complications or a total of 206. Forty-four per cent had early nonurologic, 19 per cent urologic, and 18 per cent late complications.

Comparison with similar studies is of limited value because of the innumerable uncontrolled variables which operate to compromise any conclusions. Operative technique, criteria of complications, and methods of tabulating the data would need to be accurately defined before any meaningful comparison can be made. Nevertheless, it is of some interest to note that the number of patients with complications was not materially different from that reported by Coller in 1942 and Binkley in 1947. Similarly our experience in respect to urinary complications is comparable to that of Hill and co-workers and of Marshall and associates.

Urinary retention continues to be the single most common postoperative complication and cause of prolonged morbidity. Intravascular clotting remains a common complication and was the most common cause of postoperative mortality in this group of patients. Careful preoperative evaluation of the patient with correction of demonstrated deficiencies, gentle and precise operative technique with attention to the technical considerations discussed and the correction of physiologic disturbances occurring during the operation, conscientious application to the details of enlightened postoperative care, and a continuing search for the answers to present unsolved problems will result in reduction of the morbidity and mortality of this operation.

REFERENCES

1. Binkley, G. E., and Deddish, M. R. Complications of abdomino-perineal resection of rectum for cancer. N. York State J. M., 1947, 47: 2547–2551.
2. Coller, F. A., and Eastman, P. F. Urinary retention following the combined abdomino-perineal resection. Surgery, 1943, 14: 223–228.
3. Coller, F. A., and Ransom, H. K. Carcinoma of the rectum. Surg. Gyn. Obst., 1944, 78: 304–315.
4. Goligher, J. C., Lloyd-Davies, O. V., and Robertson, C. T. Small gut obstructions following combined excision of the rectum with special reference to strangulation round the colostomy. Brit. J. Surg., 1951, 38: 467–473.
5. Hill, M. R., Barnes, R. W., and Courville, C. B. Vesical dysfunction following abdomino-perineal resection. J. Am. M. Ass., 1937, 109: 1184–1188.
6. Marshall, V. F., Pollack, R. S., and Miller, C. Observations on urinary dysfunction after excision of the rectum. J. Urol., Balt., 1946, 55: 409–416.
7. Miles, W. E. A method of performing abdomino-perineal excision for carcinoma of the rectum and of the terminal portion of the pelvic colon. Lancet, Lond., 1908, 2: 1812–1813.
8. Rankin, F. W., and Johnston, C. C. Surgical treatment of cancer of the rectum and rectosigmoid. J. Am. M. Ass., 1948, 136: 371–375.

EDITORIALS

RATIONAL SURGICAL TREATMENT OF DUODENAL ULCER

EDGAR J. POTH, M.D., Ph.D., F.A.C.S., Galveston, Texas

THE GREATEST PERCENTAGE of so-called "satisfactory results" obtained from a single surgical procedure for the treatment of duodenal ulcer follows massive resections of the stomach, but the failures following such resections are serious and frequently cause gastric crippling. Furthermore, many of the individuals considered to be improved have merely exchanged the disability of duodenal ulceration for a lesser but definite one.

Recent advances and observations made relating to results of surgical treatment of duodenal ulcer should focus our attention upon certain fundamental physiologic facts and concepts. The importance of the emotional factors mediated through the vagal and extravagal pathways must not be underestimated. The duodenal mucosa of a given individual possesses a definite tissue defense against the digestive aggression of the acid-pepsin secretion of the stomach. Gastric hypersecretion of pepsinogen and hydrochloric acid is, without doubt, the most important single direct factor causing duodenal ulceration. The role played by the prepyloric mucosa on gastric secretion cannot be overestimated. Gastric secretion may be either suppressed or stimulated depending upon the degree of acidity or alkalinity of the prepyloric antrum.

When the acid chyme of the stomach pours over the prepyloric antrum, there is inhibition of gastric secretion. Regurgitation of the alkaline contents of the duodenum upon the mucosa of the same area stimulates secretory activity. These observations are fundamental and profoundly affect our concepts of surgical treatment for duodenal ulcer. The function of the alpha cells, which are present not only in the islets of Langerhans of the pancreas but apparently also in the wall of the stomach and duodenum of man, may strongly influence peptic ulceration.

These considerations do not include all the factors which govern the pathologic physiology resulting in duodenal ulcer but must be dealt with rationally before we can hope to control this abnormal process. All of these factors must be brought into relatively normal physiologic balance if injured duodenal mucosa heals rather than develops into a chronic ulcer and progressive tissue destruction.

A duodenal ulcer will usually heal if the acid-pepsin secretion of the stomach is sufficiently reduced. An adequate gastric resection will regularly reduce the acid-pepsin factor, but, unfortunately, extensive resections may result in "physiologic cripples" who dump, lose weight, develop intractable diarrhea, or form stomal ulcers. Present and past surgical treatment of duodenal ulcer reveals these important facts: (1) Simple gastrojejunostomy will result in a 70 per cent cure rate of duodenal ulcer. (2) It is not imperative and probably undesirable to excise the ulcer in the duodenum unless it is a deep perforation on the posterior wall or active massive hemorrhage is present which

From the Department of Surgery, Service B, The University of Texas Medical Branch, Galveston, Texas.

must be controlled at the time of operation. (3) The incidence of stomal ulcer is high if the prepyloric mucosa is left as a pouch in continuity with the duodenum when a partial gastric resection is performed. (4) A vagotomy, combined with a gastroenterostomy not placed within the pyloric antrum, gives unsatisfactory results frequently. On the other hand, if the gastroenterostomy stoma is situated in the pyloric antrum, or a Heineke-Mikulicz pyloroplasty is performed, 90 per cent of patients experience satisfactory results. (5) The incidence of disability following massive resection, more than 75 per cent of the stomach, is prohibitively high among individuals who must gain their livelihood by physical exertion. Fifty per cent of these patients cannot maintain their preoperative weight. (6) Following massive resections of the stomach, the dumping syndrome is not infrequent and may be disabling. (7) Sleeve and wedge resections of approximately 50 per cent of the stomach, with preservation of the prepyloric antrum, result in a high cure rate of duodenal ulcer.

What are the common denominators in these statements? (1) Extensive resections of the stomach are undesirable. (2) Gastric secretion is inhibited if the prepyloric mucosa is exposed to an acid environment. A duodenal ulcer will usually heal if the acid-pepsin secretion of the stomach is suppressed sufficiently during the nondigestive phase. (3) The cure rate of duodenal ulcer following vagotomy is largely dependent upon the location of the gastroenterostomy stoma in the pyloric antrum. This arrangement will render the greater portion of the prepyloric mucosa acid while most of the irritating acid gastric secretions will be shunted away from the duodenum. Conversely, if the gastroenterostomy stoma is situated on the greater curvature of the stomach at a considerable distance from the pylorus, or if the stomach is divided and the distal segment closed so as to form a pouch lined by prepyloric mucosa in proximity with the duodenum, allowing the alkaline secretions of the duodenum to regurgitate up upon the prepyloric mucosa stimulating secretion of gastrin and increased gastric secretion, the duodenal ulcer heals, but, a stomal ulcer develops.

Some of the failures following vagotomy, combined with a correctly situated gastroenterostomy stoma or a pyloroplasty are possibly due to the presence of a sensitive extravagal central pathway stimulating gastric secretion excessively. This mechanism is demonstrable often by gastric analysis during insulin induced hypoglycemia. It is interesting that vagotomy and gastroenterostomy, combined in a single operation, yield a 90 per cent cure rate, while the cure rate is considerably higher if the gastroenterostomy is performed initially and followed by vagotomy subsequently in the 30 per cent of patients not benefited by the first procedure. Vagotomy performed for stomal ulcer following gastroenterostomy gives a 90 per cent satisfactory result. If the same cure rate follows vagotomy, regardless of why the gastroenterostomy fails, then the combined cure rate would equal 97 per cent.

The mechanism responsible for failure following vagotomy combined with gastroenterostomy may be due to the hypothalamic stimulation of the pituitary to give ACTH, and so stimulate the adrenal cortex to form adrenal cortical hormones which then stimulate the parietal cells of the stomach to secrete excessively. The hypothalamus may have been activated initially either directly by preprandial hypoglycemia or indirectly by hypoglycemic stimulation of the adrenal medulla to secrete epinephrine which then acts on the hypothalamus. When the stomach is empty, gastric hypersecretion is more prone to induce recurrent ulceration. It is important to demonstrate if such secretory activity exists.

I have, for several years, used an analytical procedure designed to determine gastric secretory activity when the stomach is empty. It is tedious and time-consuming but gives valuable information. The procedure is divided into two phases: a 12 hour resting

period followed by stimulation with intravenous insulin. Blood sugar levels are determined and the gastric specimens are examined for free acid, total acid, and hydrogen ion concentration as well as volume. After the blood sugar has returned to normal, a secondary rise of gastric secretion occurs, which is interpreted as being due to stimulation via the hypothalamic, pituitary, adrenocortical mechanism. The intravenous administration of glucagon, the hormone secreted by the alpha cells found in the islets of Langerhans, induces a gastric response similar to this same mechanism. Occasionally, these changes are pronounced. Renal excretion of 17-hydroxycorticosteroids is increased following the intravenous administration of glucagon. The extravagal pathway, including a hyperactive adrenal cortex, could be the mechanism responsible for the occasional failures following vagotomy combined with gastroenterostomy or pyloroplasty.

Individuals suffering from hyperthyroidism seldom develop duodenal ulcer, although these individuals are admittedly highly nervous and emotionally unstable. The diminished urinary excretion of 17-ketosteroids indicates a reduced adrenocortical activity and may well suggest the importance of the adrenocortical mechanism in peptic ulceration.

The foregoing observations logically suggest multiple stage operations for duodenal ulcer. The first stage should be a simple operation altering the anatomy and physiology as little as possible to be followed by a second stage operation for those patients in whom the first stage proves inadequate. The first operation should be the simplest procedure which could be expected to yield a reasonable cure rate. A gastroenterostomy with the stoma placed near the pylorus would be a rational procedure. Inhibition of the hormonal phase of gastric secretion by the mucosa of the duodenum and pyloric antrum, when bathed by an acid medium, would be preserved. None of the patients subjected to this first operation would permanently become "gastric cripples." The small residual group would present the serious problems and require special study. Gastric secretion can be reduced further by the sleeve or wedge resection of 50 per cent of the stomach with preservation of the pyloric antrum. These patients may include those individuals with highly sensitive extravagal, central mechanisms for gastric secretion, those having increased activity of the alpha cells of the islets of Langerhans and of the gastroduodenal and visceral walls, and those who are emotionally unwilling or economically unable to follow the habit pattern demanded of a duodenal ulcer patient.

The true influence of the adrenal cortex, through several mechanisms, on duodenal ulcer disease is not yet established, but its possible importance should be kept in mind.

Let us analyze statistically three hypothetical groups of 100 patients each.

The first group is treated by staged procedures: (1) gastroenterostomy, with the stoma in the pyloric antrum: 30 unsatisfactory results; (2) subsequent vagotomy: 3 to 5 unsatisfactory results; (3) mortality 1.5 per cent: 130 operations, 2 deaths.

The second group is again treated by staged procedures: (1) vagotomy with gastroenterostomy or pyloroplasty: 90 per cent satisfactory; (2) subsequent sleeve or wedge resection of 50 per cent of the stomach on the 10 failures; (3) mortality: 110 operations, 2 deaths.

Groups 1 and 2 yield essentially the same results. Would the procedures used in the second series be superior to those of the first group because 20 per cent of the individuals would be spared a second operation although 10 per cent should be subjected to 50 per cent gastric resection?

The third group is treated by massive (75 per cent or more) gastric resection: (1) gastric resection, 7 unsatisfactory results; (2) mortality 5 per cent, 5 deaths. The results from massive gastric resection are not superior. There is irreparable loss of stomach; little can be done to correct the failures in patients who are essentially gastric cripples,

and the mortality is twice as great. There has been minimal alteration of the anatomic and physiologic functions in the first group and further avenues of treatment are still open.

Although the best detailed course to follow is not evident, the rational surgical treatment of duodenal ulcer includes certain essential considerations. First, do not perform extensive resections of the stomach as an initial procedure. Second, accept the concept of staged operations for duodenal ulcer. The first stage would shunt the major portion of the gastric secretions away from the duodenum with minimal alteration of the anatomy and physiology of the stomach. This relatively minor operation will relieve a large percentage of the patients. Subsequent vagotomy would reduce the unsatisfactory results to a small number. Finally, the failures should be studied meticulously and treated by a more extensive and ambitious program. Every effort should be made to preserve the physiologic mechanisms which inhibit gastric secretion. Seldom will gastric resection exceeding 50 per cent of the stomach be indicated. Multiple operative procedures are time-consuming, expensive, and a nuisance to the surgeon, but "gastric crippling" is a major catastrophe for the individual patient.

THE SURGEON RETIRES

ALLEN O. WHIPPLE, M.D., F.A.C.S., Princeton, New Jersey

THE QUESTION OF TIME is very involved both as to its meaning and its effect on us as individuals. John Buchan once said "As we age, the mystery of time more and more dominates the mind. Time goes on and for us mortals in only one direction." However, this time motion has been disputed. Four hundred years ago, Rossand said "Time goes you say? Ah no, alas, Time stays, we go." Today the superscientists review the cosmos as a time space continuum, and time and space as a constant. To the relativity of time, motion, and space Einstein has contributed more than anyone else. This idea is better explained by the following:

> There was a young lady so bright
> She travelled much faster than light
> She went out one day, in a relative way,
> And came back on the previous night.

Nevertheless our years accumulate, and as Mark Twain remarked on the weather "There's nothing we can do about it." But the wear and tear of the surgeon's work too frequently imposes retirement rather than his advanced years. What I wish to discuss are the compensations of retirement and preparing for it.

Now as to the compensations: Time is your own for the first time in many years to do with it as you please, and a rare experience after the busy life and heavy responsibilities of the surgeon. No more early ward rounds. No more midnight and two o'clock emergency calls. No more anxious hours before, during, and after critical operations, and trying times with the distraught and unreasonable members of the family of the patient and his critical friends who think they are influential. No more dull and interminable committee meetings.

Now there is time to follow pet hobbies, to read many books on many subjects that one has not had time for in years gone by. Time to resume investigative problems, previously attempted or contemplated. Time to sit quietly and review leisurely the happy incidents and experiences of a surgical career. And there is time to contemplate with tranquility and with faith the sunset and twilight of life.

Much can be done in preparing for retirement, and it must be done before it is too late. Retire while still competent, before senescence has a chance to go into senility. Senescence, by the way, begins at birth. You may and should choose a number of things in preparation, though your choosing does not necessarily mean getting. One should choose his parents and early environment—not always possible!

Choose good health and a strong constitution. This makes for a longer and a more enjoyable retirement. But even if you have indulged in a coronary or two, don't let it get you down. I knew, and had several years of dear friendship with a most charming and distinguished physician. At the age of 60 he had a coronary, which his doctors told him made retirement mandatory. So he retired and very wisely took up ornithology as his avocation, and turned his ample grounds into a bird sanctuary. For 20 years he played this hobby and became a national figure in the study of birds. His stories about his birds were truly fascinating.

Choose your associates. What a difference that choice will make in your work as a surgeon and in your friends and memories later. And by all means marry the right girl. The wife can help or hinder you in your work and your life in retirement. A surgeon's wife has a hard life and too seldom gets deserved credit for the success of her husband in his too busy life.

Choose your avocation and hobbies. Hobbies do not have to be elaborate or expensive. Some of them are hard to understand, such as hunting and collecting epitaphs from mouldering tombstones. They do not have to be gloomy. They should be interesting and absorbing to the individual, and if possible to his family. If you paint or sculp or carve wood or play a musical instrument, you do not have to exhibit the results, not even for the family's admiration, although that does help. The temptation to exhibit the results often needs curbing.

Tying flies or painting landscapes has the advantage of being less noisy than practicing on a cello, and they favor contemplation too. Of course, some hobbies and avocations are of great assistance in the transition from a busy surgical practice to the life of Riley. There is nothing more tragic than watching a surgeon, especially one that has been a showman, with no other interest than operating, turning into an uninteresting vegetable when chronic disease or old age compels him to retire.

Choose a good place to live in when you retire, so that you can have time and place for your avocations, and where you will have friends with mutual interests and friendly understanding. You may find one or more peculiar fellows to play chess with, not too strenuous a game, but one not equaled by any other for keeping your mind keen and alert.

Finally, be sure that you have a nest egg laid aside for the years of retirement, for yourself and your family. And be content to live modestly. A large income may prevent you from having an enjoyable and peaceful retirement.

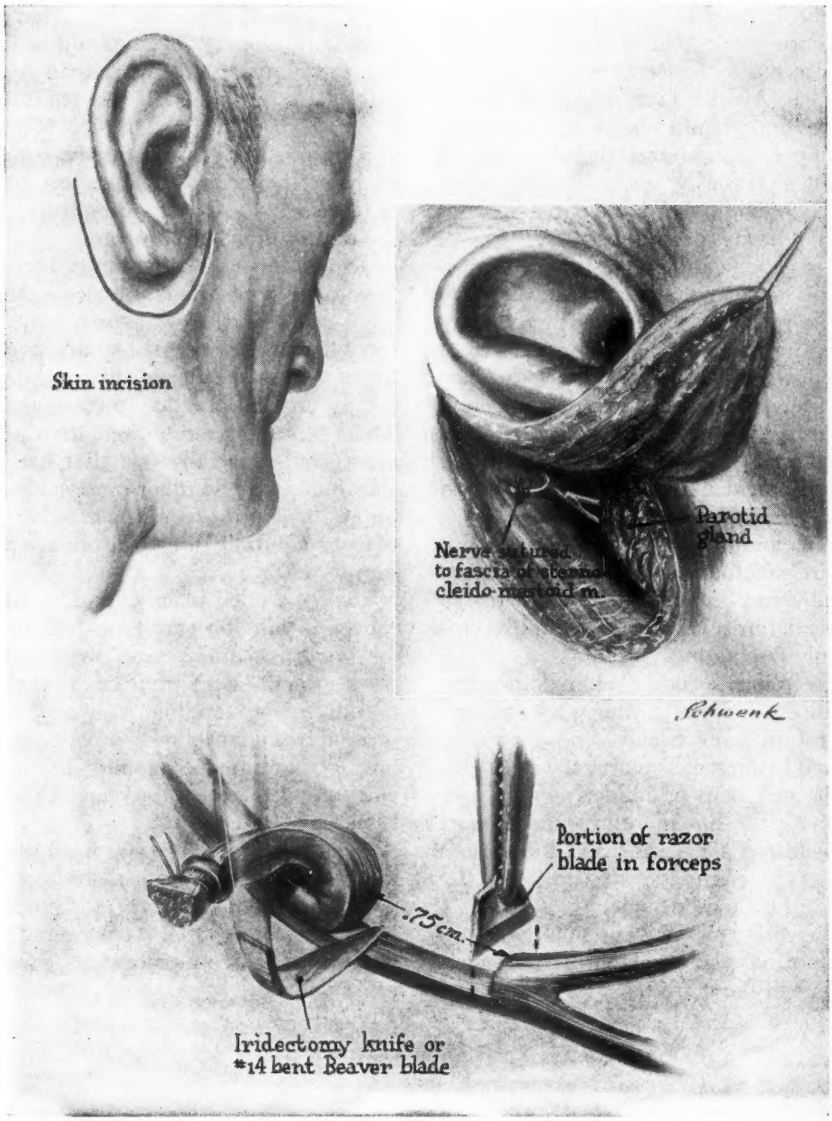


FIG. 1.

Partial Section of Proximal Seventh Nerve Trunk for Facial Spasm.—W. B. Scoville.

THE SURGEON AT WORK

PARTIAL SECTION OF PROXIMAL SEVENTH NERVE TRUNK FOR FACIAL SPASM

W. B. SCOVILLE, M.D., F.A.C.S., Hartford, Connecticut

HEMIFACIAL TWITCHING OR TIC is not uncommon and proves a most fatiguing and embarrassing disability, generally found in middle or older age persons having cerebral arteriosclerosis or hypertension. Numerous surgical procedures have been described for its relief including alcohol block, sectioning with resuture, sectioning of the ocular branch, and decompressive operations and cross-anastomoses. None of these procedures has proved satisfactory because of too much initial paralysis followed by an early return of spasm or mass reaction. German in 1942[1] described the most satisfactory method to date with partial sectioning of each of three branches of the facial nerve distal to the parotid gland. This method presents certain technical difficulties and frequent early regeneration. The author has tried out a new technique based upon German's work, with partial sectioning of the seventh nerve in its main trunk just distal to the stylohyoid foramen and just proximal to its first main branching. This operation has now been performed on 6 patients with unilateral facial tic. The late results have been sufficiently gratifying and the follow-up period long enough to warrant this report.

TECHNIQUE

It is imperative that the operation be performed under local anesthesia with the facial muscles under observation. With the patient on his side an incision is made around the inferior edge of the ear, and the facial nerve is exposed at its exit from the stylohyoid foramen by exposing the anterior edge of the sternomastoid muscles followed by blunt dissection to deeper planes with a Kelly hemostat and the use of a localizing nerve stimulator (Fig. 1). Additional aids can include chiseling off the tip of the mastoid or exposing the digastric muscle and its small nerve branch from the seventh nerve which can be followed proximally to the seventh nerve trunk proper. The main trunk of the seventh nerve is exposed and freed to its primary branching which lies 1 to 2 centimeters distal to the mastoid bone and just under the edge of the parotid gland. A self-retaining retractor is used. A small square of sterile tongue stick or other hard, smooth surface is placed under the nerve trunk, and the nerve trunk is sectioned approximately ⅔ through its total diameter beginning at its superficial surface. The sectioned portion is then ligated tightly, turned back on itself and stripped for a distance of ½ centimeter, and sutured to the sternomastoid muscle. This partial sectioning of the nerve trunk can be carried out with a bit of razor blade held horizontally in a mosquito hemostat. To prevent the danger of inadvertently cutting too deeply one may prefer first to insert a right-angled bent 27 gauge hypodermic needle through the nerve trunk and cut down on this needle with the razor blade; or one may first slit the nerve horizontally with a small bent Beaver blade or with the stylet of the hypodermic needle transfixing the nerve trunk after removing the needle proper. This stylet can be grasped on either side of the nerve by mosquito hemostats and slid longitudinally to split the nerve. The superficial half of the nerve is then cut with tiny scissors. If possible, the distal, cut fibers should also be tied. Because of this

[1]GERMAN, W. J. Surgical Treatment of Spasmodic Facial Tic. Surgery, 1942, 11:912.

nerve's known propensity for extreme regeneration, a good two-thirds of the thickness should be sectioned until a visible near paralysis of both the orbital and mouth muscles has occurred, the patient being barely able to close his eyes or show his teeth. By experiment the author has found that it makes no difference if one sections the superficial or the deep surface of the trunk so long as some fibers are left intact which run to both main branches. Hence, the sectioning must be done just proximal to its primary branching. Closure is effected with finest silk throughout without drains, and the patient is allowed up at once. There will be a very appreciable paresis of the facial musculature lasting on an average of 3 months, but regardless of the degree of paralysis all patients have shown a return to normal function in several months' time.

CASE REPORTS

Case 1. N. K., a 49 year old male, for a year had had a progressive left facial spasm closing the eye completely, rhythmic click in the ear, and pain and twitch of the occipitalis muscle. His blood pressure was 170/118. He had had previous nerve injections, occipital neurectomy, and the German procedure, with complete recurrence at 22 months. A second facial nerve operation was performed on June 7, 1948 and all four branches anterior to the parotid gland were again sectioned, this time *totally*, without stopping the twitching. Then a partial section through the superficial surface and one-half the diameter of the trunk was carried out proximal to the initial branching. Temporary paralysis of lower facial muscles returned in 3 months as well as mild (30 per cent) twitching of the lower eyelid and of the upper lip in 1¾ years which has been stationary since then to date—6½ years. There is a permanent weakness of the risorius muscle due to previous surgery on the nerve distal to the parotid gland. The result is fair to good.

Case 2. J. L., a 46 year old woman, had had a neurotic "habit spasm" tic for 1 year following a liability case which resulted from being jarred in a store elevator in 1945. Her blood pressure was 196/120. Operation was performed on December 16, 1949 with experimental sectioning through the deep or undersurface of one-half the diameter of the main trunk of facial nerve. Partial paralysis existed for 3 months; she was normal without tic for 1 year; then had a 50 per cent recurrence. She has moved to another state and wishes to delay reoperation. There has been an intermittent return of the twitching due to inadequate section of the undersurface of the nerve which necessitates a more difficult operation. The result is poor.

Case 3. P. L., a 42 year old, extremely obese woman, had had severe hypertension requiring thoracolumbar sympathectomy and progressive facial twitching over the previous year. Operation was performed on December 16, 1949, with partial sectioning through the superficial surface and one-half the diameter of the facial nerve trunk just proximal to its initial branching. She had almost complete paralysis for 2 months and 100 per cent return of function in 5 months. There was a minimal fine tremor of the lower eyelid only during hypertensive bouts beginning at 1 year. There has been no further progression to date at 5 years. The result is good.

Case 4. C. B., a 49 year old woman, had moderate tic that had been progressive over 12 years. Her blood pressure was 148/96. Operation was performed on August 2, 1951 with partial sectioning through the superficial surface and three-quarters of the diameter of the facial nerve trunk proximal to initial branching. There was a 75 per cent paralysis for 1 month postoperatively with recovery in 3 months and the slightest tremor of lower eyelid at 2 years when tired. She is cured now at 3 years. The result is excellent.

Case 5. F. C., a 58 year old woman, had marked hypertension. Her blood pressure was 220/120. There was progressive spasm of the eye more than mouth during the previous year. Operation was performed on July 2, 1952 with partial sectioning through the superficial surface and two-thirds of the facial nerve trunk proximal to its initial branching. There was temporary nearly complete paralysis for 2 weeks with 50 per cent recovery at 1 month and complete recovery at 3 months. There has been no recurrence of tic for 2 years. There has been a 25 per cent recurrence in the eyelid only at 2¼ years. The result is good.

Case 6. F. G., a 58 year old man with normal blood pressure (116/70), had a 5 year history of moderate facial tic of the eye more than the mouth. Operation performed on February 16 and 18, 1953 was complicated by drug sensitivity requiring general anesthesia. Insufficient sectioning was performed through the superficial surface and one-third of the diameter of the facial nerve trunk with continuing fine tremor of the left lower eyelid. Hence, further sectioning was carried out 2 days later through approximately three-quarters of the diameter of the nerve trunk. It was feared that too deep a section had been done causing a paralysis of the left side of the face which lasted 6 months, but a spontaneous complete recovery occurred at end of that time with cure of the tic for 1¾ years. The patient now shows a 25 per cent return of tremor of the lip only, whereas previously the eyelid had been more involved. The result is fair to good.

RESULTS

Late results in Case 1 can be considered fair, complicated by 2 previous operations on distal

branches and inadequate partial sectioning of the main trunk. Late results in Case 2 are poor because of an inadequate experimental sectioning of the deep or inner surface of the nerve trunk (technically more difficult). She was cured for 6 months with some 75 per cent recurrence since, and should have a repeat operation. Late results in the last 4 patients (Cases 3, 4, 5, and 6), with 2 to 6 year follow-ups, can all be considered good with a mild return of intermittent tremor and quivering of the lower eyelid under fatigue in 2 patients, of the lip in 1 patient, and a complete cure to date at 3 years in another patient.

DISCUSSION

The operation herein described offers the following advantages: (1) a hidden scar; (2) greater facility of exposure and of sectioning than in the more distal procedures; (3) a degree of recurrence which appears to be considerably less and more delayed than in other procedures; (4) greater ease of reoperation when necessary; (5) retention of discrete functions which are lost in complete section plus resuture, and in anastomotic operations.

Partial section of the proximal trunk does not appear to affect one division more than another, suggesting incomplete orientation of fibers at this level; for this reason, consideration will be given toward resecting a portion of the trunk intracranially at the cerebellopontine angle in future cases. A very slight mass reaction of split axon regeneration is noted in all cases indicating some regeneration of the cut fibers, but it is far less than seen in complete sections or anastomotic operations.

CONCLUSIONS

Late results have exceeded the expectation of the author. Manifest failures have been due to technical inadequacy of the section. A small amount of recurrence, generally 25 to 35 per cent, intermittent under fatigue and involving the eyelids, must be anticipated at 2 to 4 years' time, a longer time interval than occurs in other surgical approaches. Recurrence sufficient to warrant reoperation has occurred in 1 early case.

SUMMARY

1. A method of partial sectioning of the proximal extracranial portion of the seventh nerve is described for the treatment of facial tic.

2. Presentation is made of 6 cases in which this operation was performed and which have been followed from approximately 2 to 6½ years.

3. Late results have been excellent in 1 patient, good in 3, fair in 1, and poor in 1, respectively. Results in the latter 2 patients are believed to be due to inadequate surgical sectioning in the earlier operations.

4. A temporary paresis of the facial muscles for 3 months and a late mild return of eyelid tic under fatigue are to be expected at 2 to 4 years.

5. There have been no complications nor permanent weakness.

The Book Shelf

JAMES DOUGLAS AND THE PERITONEAL CUL-DE-SAC

HAROLD SPEERT, M.D., F.A.C.S., New York, New York

THE CUL-DE-SAC is the rich domain of the gynecologist. Through its thin walls he palpates the pelvic viscera, ascertaining the size and position of the uterus and adnexa, outlining pelvic masses, and eliciting areas of tenderness, and plunges the culdescope for visualization of the pelvic contents; from its recess he drains pus in the treatment of pelvic abscess and aspirates blood in the diagnosis of ectopic pregnancy; he incises its trough in the performance of vaginal hysterectomy, and approximates its walls in the repair of enterocele.

Inseparably identified with this pouch of the peritoneum is the name of James Douglas, who first described it in 1730 in his famous treatise, *A Description of the Peritonaeum* (Figs. 1 and 2). Less than a paragraph, however, was devoted by Douglas to the structure with which his name is now so constantly associated; little did he surmise the importance that subsequent generations would attach to it. Today many gynecologists, notably among the Germans, drop the word "pouch" in referring to the cul-de-sac and speak of it merely as "the Douglas."

Nowhere in Douglas' description are the terms pouch or cul-de-sac to be found. In fact, the French compound did not achieve its first use in the English language until 1737, 7 years after the publication of Douglas' book, when Alexander Monro, Professor of Anatomy in the University of Edinburgh, employed the term, in its present anatomic meaning, in describing the relations of the pelvic colon. Cul-de-sac is now used to denote any kind of blind alley or dead end. "At the Part of the Mesocolon," wrote Monro, "which connects the sigmoid Flexure of the Colon near the left Cavity of the Ilia, where in most adult Bodies there is an *Infundibiliform Cul de Sac*, or *Thimble-like* Cavity, I could never observe in Children more than one Part of the Mesocolon laid over the other, because of the great Flexure of the Gut at this Place; and therefore conclude the Cavity to be accidentally formed, by the growing together of the contiguous Parts of the *Mesocolon:* And that it is as needless to assign Uses to it, as it would be, to shew how useful the Concretion of the Lungs and *Pleura* is, which seldom misses to be observed greater or less in adult Bodies."

The peritoneal cavity had been described as early as 3,000 B.C., in the *Ebers Papyrus*, as a space in which the viscera are somehow suspended but little was added to its understanding until Douglas' monumental work. Even then, Douglas' description received but scant attention, for abdominal surgery was still unknown, except for paracentesis and cutting for the stone. In his prefatory dedication of his book to Dr. Mead, Physician to His Majesty, Douglas stated: "It is now many Years since I first had the Honour to discourse with you concerning the Situation and Structure of the Peritonaeum; neither of which have, in my Judgment, been hitherto rightly described. When I began my

From the Department of Obstetrics and Gynecology, Columbia University, New York.

Inquirys about this important Membrane, I had the Aetiology of several Diseases principally in view; among which were Dropsys, Hernia's, and some other accidents peculiar to Women."

Douglas' views on the anatomy of dropsy proved to be erroneous. He thought that the ascitic fluid collected in the "vesicular substance" lying between the anterior peritoneum and the transversalis fascia, and as it increased, pushed the peritoneum backward, thereby compressing the intestines against the vertebrae.

By contrast, his interpretation of umbilical hernia and omphalocele was remarkably accurate: "A fourth Production not always distinctly visible in Adults, reaching from the Navel of the Anteriour Point of the Bladder, contains the Urachus. So that in reality, all these Vessels are situated in the same manner with respect to the Peritonaeum, as the Viscera which are universally said to lie in its cavity. But what is still more observable about these Vessels is, that the Peritonaeum accompanys them through the Umbilicus out of the Abdomen of the Foetus, and thus becomes an Involucrum to the Funis Umbilicalis all the way to the Placenta. This may be easily exhibited to view in any proper Subject; but it became remarkably plain in a Child that I lately examined, in whom a Hernia Umbilicalis had been formed in Utero. Part of the Intestine was near two inches without the Navel, and the Peritonaeum which accompanied it, was evidently continuous with the Involucrum of the Funis."

Douglas' lucid explanation of the visceral and peritoneal relations has not been improved upon to this day: ". . . Concerning all the other viscera [except the omentum and part of the liver], it is to be observed, that no part of them immediately touches the Internal or concave smooth Surface of the Peritonaeum, and consequently they cannot be said to be contained in its Cavity, as Liquor is in a Bottle, Money in a Purse, or in short, as any thing, whether Solid or Liquid, is in a Cafe, Bag, or Vessel, that simply surrounds it. To conceive therefore the Manner in which this is done, we must imagine the Peritonaeum as a Bag of a much larger Extent and Capacity than the Cavity of the Abdomen; and that the Viscera it contains being applyed to several Parts of its external Surface, thrust its yielding sides inwards, till at length the Edges of the Cavitys so formed by each Viscus, come to touch one another. Thus will the Capacity of the Peritonaeum be diminished in Proportion to the Number and Size of these Viscera; and each of them may be justly said to be contained in its Cavity, not only as they form particular Cavitys to themselves, where the Peritonaeum separately involves them, but as they all lie within the one common Cavity of the Abdomen lined by the Peritonaeum, considered as an uniform Membrane, without any regard to the particular Productions of it, which surround each viscus. From hence it is evident that the external Surface of the Peritonaeum alone is contiguous to the Surface of the Viscera contained herein . . ."

James Douglas, brother of John Douglas the surgeon, was born in Scotland in 1675, but the details of his early life and training are little known. There is not even a portrait of this important figure recorded in any of the great libraries and portrait galleries of Scotland, Eng-

A

DESCRIPTION

OF THE

PERITONÆUM,

And of that Part of the

MEMBRANA CELLULARIS

Which lies on its OUTSIDE.

WITH

An ACCOUNT of the True Situation of all the ABDOMINAL VISCERA, in reſpect of theſe two Membranes.

BY

Dr. *JAMES DOUGLAS,*

Phyſician in Extraordinary to HER MAJESTY, Honorary Fellow of the Royal College of Phyſicians, *London,* and Fellow of the Royal Society.

LONDON:

Printed for J. ROBERTS, near the *Oxford-Arms* in *Warwick-Lane.* M. DCC. XXX.

FIG. 1. Title page of Douglas' book on the peritoneum.

(37)

the two Inciſions, the *Meſentery* forms a ſort of longitudinal *Septum* going between the *Inteſtines* and *Peritonæum*, and likewiſe another narrower Portion round the Edges of the ſmall Guts, which is chiefly between the *Peritonæum* and *Colon*, being that part of the *Meſentery* termed *Meſo-Colon*. In this View of the *Peritonæum* we likewiſe perceive, that having reached as low down on the *Vertebræ* as the laſt of the Loins, it ceaſes to ſurround the *Inteſtinum Rectum*, or, perhaps, the End of the *Colon* intirely, the poſteriour ſide thereof being covered only by Veſicular Subſtance; and this bare ſpace increaſes in breadth as it deſcends; the anteriour ſide of the Inteſtine remaining ſtill covered by the *Peritonæum* all the way down to where it comes neareſt to the *Veſiculæ Seminales:* below this it is intirely ſurrounded by a thick Veſicular Subſtance, which here, if any where, deſerves the Name of *Membrana Adipoſa*, becauſe of the vaſt Quantity of Fat contained in it. Where the *Peritonæum* leaves the foreſide of the *Rectum*, it makes an Angle, and changes its Courſe upwards and forwards over the Bladder; and a little above this Angle, there is

a

(38)

is a remarkable tranſverſe Stricture or Semi-oval Fold of the *Peritonæum*, which I have conſtantly obſerved for many Years paſt, eſpecially in Women.

Spleen and Pancreas. WHAT has been ſaid of the Stomach may likewiſe be applyed to the Spleen and *Pancreas*, both of them being involved by the *Peritonæum*, produced from where they are contiguous to it. The firſt is ſeated in the left ſide of the *Abdomen* nearly according to the length of the Body, reaching from the Diaphragm down below the Extremity of the twelfth Rib; the other lies almoſt tranſverſely on the firſt *Vertebra* of the Loins, above half of it being towards the left ſide.

Liver. The Liver has this peculiar to it, that a large Portion thereof is immediately joyned to the internal Surface of the *Peritonæum*, *viz.* all the ſuperiour and back part of its convex Surface, which lies to the right of the *Ligamentum Latum*. This adheres cloſely to part of the *Peritonæum* that lines the Diaphragm, the reſt of it is involved in the ſame manner as the other *Viſcera*, by means of ſeveral Folds which go from the *Peritonæum* in form of Ligaments, and are afterwards ſpread on its

b

FIG. 2. a and b, Excerpt from *A Description of the Peritonaeum* containing Douglas' description of the cul-de-sac.

land, or the United States. After obtaining his medical degree in Rheims, Douglas settled in London, about 1700, where he developed a large and lucrative obstetric practice while carrying on his anatomic investigations. He ultimately achieved the position of personal physician to Queen Caroline.

In the winter of 1726 Douglas, together with Sir Richard Manningham, brought about the exposure of Mary Tofts, a poor journeyman clothier's wife, who had achieved recent fame by professing to have borne large litters of rabbits. Of Mary the imposter's confession, Sir Richard later wrote: "Accordingly on Wednesday December 7, in the Morning, in the Presence of . . . Dr. Douglas and myself, she began her Confession of the Fraud; and in her Confession she own'd, That upon her miscarrying she was seized with violent Floodings, and the womb was then . . . open as if she had been just deliver'd of a full-grown Child, she did verily believe one of her wicked Accomplices did then convey into her Womb part of the Monster . . . being the Claws and Body of a Cat and the Head of a Rabbet; this put her to much Pain: After that time she believed nothing was ever put into her Womb, but into the Passage only, by the Advice of a Woman Accomplice . . . who told her she had now no occasion to work for her Living as formerly, for she would put her in a Way of getting a very good Livelihood, and promised continually to supply her with Rabbets, and should therefore expect part of the Gain . . . The Woman told her she must put up her Body so many pieces of Rabbets as would make up the Number of Rabbets which a Doe Rabbet usually kindles at one time, otherwise she would be suspected. Mary Toft asked how many that was; the Woman told her, sometimes thirteen.

"From that time Mary Toft did often, by the Assistance of that Woman, convey parts of Rabbets into her Body, till at last she could do it by herself, as she had an Opportunity to do so."

Douglas shortly thereafter published his own version (2) of the investigation, concluding with the statement: "I hope all breeding Women will depend on this as a certain Truth, that it is no less probable, that a Rabbit should conceive and

be deliver'd of a Human Child, than that any Creature whatever, of an entirely different species, should be form'd in the Belly of a Woman."

Among Douglas' pupils were Albrecht von Haller and William Hunter. The latter came to live with Douglas in 1741, to assist in the dissections and supervise his son's education. Douglas died just 12 months later, however, April 9, 1742, leaving also a daughter, Martha Jane, with whom Hunter had in the meantime fallen in love; but she too died 2 years after, at age 28.

In addition to his anatomic researches Douglas maintained a lively interest in botany, publishing papers "On the Flower of Crocus Autumnalis" and "On the Kinds of Ipecacuanha," a book entitled *Lilium Sarniense, or a Description of the Guernsey Lily*, and a full description of the coffee plant, including an account of the growth of the use of coffee as a beverage in England from its introduction during the reign of Charles I. Douglas was also noted as a bibliophile, his library containing the most complete collection of the editions of Horace in existence.

His reputation as an obstetrician was immortalized by Pope in *The Dunciad:*

> There all the Learn'd shall at the labour stand,
> And Douglas lend his soft, obstetric hand.

REFERENCES

1. Dictionary of National Biography. L. Stephen and S. Lee. 4th ed., pp. 1234–1236. New York: The Macmillan Co., 1908.
2. Douglas, James. An Advertisement Occasion'd by Some Passages in Sir R. Manningham's Diary Lately Publish'd. London: J. Roberts, 1727.
3. Idem. A Description of the Peritonaeum, and of that Part of the Membrana Cellularis Which Lies on its Outside. Pp. 37–38. London: J. Roberts, 1730.
4. Graham, H. Eternal Eve. P. 308. New York: Doubleday & Co., 1951.
5. Manningham, R. An Exact Diary of What Was Observ'd During a Close Attendance upon Mary Toft, the Pretended Rabbet-Breeder of Godalming in Surrey From Monday Nov. 28, to Wednesday Dec. 7 Following. Together with An Account of Her Confession of the Fraud. London: Fletcher Gyles, 1726.
6. Monro, A. Miscellaneous Remarks on the Intestines. Medical Essays and Observations, rev. ed., 1737, 4: 76–92.
7. Oughterson, A. W. James Douglas and the Surgery of the Peritoneum. Yale J. Biol., N. Haven, 1930, 2: 331–339.

Reviews of New Books

THE SECOND SECTION of *A Stereoscopic Atlas of Human Anatomy*[1] by David L. Bassett, Associate Professor of Anatomy at Stanford University, may be enthusiastically recommended to students, teachers, and practitioners as a brief, highly accurate, and superbly pictorial survey of human anatomy, executed with technical skill and presented with artistic judgment.

As C. H. Danforth points out in his Foreword, "Everyone concerned with human anatomy has frequent occasion to refresh his mind on one or another aspect of the subject, but it is not often that he can view the appropriate dissection at a moment's notice." Continuing, he assures the reader that, "the present atlas makes this possible to a greater degree, and in a more pleasing form, than anything of its kind thus far devised"; for "here the student or the clinician can review a single dissection, a series of steps in a carefully planned exploratory sequence, the delicate internal architecture of a bone, or an illusive fiber tract, all in full perspective and in the coloring of well-preserved laboratory material." To every aspect of Danforth's commendatory statement it is a pleasure to agree with heartiest approval.

A fully labelled sketch, based upon a tracing of the original photograph, furnishes a topographic guide for each view; the views themselves are not marred by pins, numbers, or guidélines. The stereoscopic pictures record, with almost unbelievable faithfulness, essential and unobstructed perspective; exceptionally fine illumination of deep-lying structures, recesses, pneumatized areas, and foramina aids in contributing naturalness to the dissection field.

The set is compact, the views readily accessible; the views may be regrouped to answer the needs of regional review; selected elements of the present lot may, later, be interpolated on the basis of system, in sets which the author and publisher plan to provide.

The present set of views make up Section 2 of *A Stereoscopic Atlas of Human Anatomy*. It covers every important feature of cervical and capital anatomy not accounted for in Section 1. This second division of a most ambitious atlas consists of 343 three-dimensional kodachrome transparencies in full color, on 49 reels. The circular reels are stored conveniently in numbered slots at the back of each of the several volumes of text. A table of contents, like that of a textbook, lists the title of each view and the features illustrated in each view. The reels are accompanied by text, which presents pertinent information, and by drawings, each of which is amply and clearly labelled.

The reels of pictures are to be used with Sawyer's View-Master stereoscope. Thus, the pictures may be studied by the individual or may be projected on a screen, for instruction of classes and seminars in school, hospital, or clinical meeting.

Bassett's enviable experience as a teacher and his rare ability as a critical anatomist would, of course, guarantee the quality of this set. He is most fortunate in having the technical collaboration, in the capacity of photographer, of William B. Gruber, designer of the stereoscope which accompanies the reels and text. Mr. Gruber's skill is as essential to such an endeavor as the ability of an artist is to the anatomist who prepares a textbook or atlas of the more familiar kind.

For the second step in the progress of this monumental endeavor, there could be nothing but the most enthusiastic praise. —*Barry Anson.*

THE "GOLDEN PERIOD" is the first few hours presented to the surgeon following acute hand injury. The frequent and ubiquitous occurrence of hand injuries thus presents a "golden period" to many surgeons. If methods and techniques as presented by H. Minor Nichols in the *Manual of Hand Injuries*[2] are followed, the "golden period" will be less tarnished.

The book presents the advantages of compactness—352 pages with 180 illustrations, and in book size, 6 by 9 inches—small enough to find ready place in the hospital locker as well as the library shelf.

The first chapter includes anatomy of the hand and forearm, a convenient inclusion, for the occasional operator, to have in a book dealing with acute care. The anatomic drawings are adequate but lack somewhat in yielding to the reader a sense of third dimensional depth.

The second chapter on general technique is well covered. Some readers may wish that the author had given stronger warning against the use of local anesthesia by direct injection and digital nerve block at the base of the fingers, and emphasized that anesthesia in these same areas can be adequately obtained by median, radial, and ulnar nerve blocks at wrist level.

The chapter on minor injuries is well covered and practical.

The chapter of traumatic amputations emphasizes the value of saving lengths and finger tip pulp. The author has chosen not to include a discussion of cross-finger flap technique in traumatic amputations. This may be appropriate, for the procedure, though valuable, demands more in the way of technique than the occasional operator may have an opportunity to bring to bear on this problem.

In the chapter on the treatment of hand burns, the author properly favors for initial treatment the occlusive type dressing with the hand splinted in the position of function. The value of elevation of the hands in the early part of treatment is not stressed; this might well be emphasized.

The chapters on skin grafting and primary flap grafts are excellent for clarity of the basic techniques explained. So also are those on tendon muscle injuries and nerve injuries.

[1] A STEREOSCOPIC ATLAS OF HUMAN ANATOMY. Section 2—HEAD AND NECK. By David L. Bassett, M.D. Reels 35–44. Color photographs by Wm. B. Gruber. Portland, Oregon: Sawyer's, Inc., 1954.

[2] MANUAL OF HAND INJURIES. By H. Minor Nichols, M.D. Foreword by Michael L. Mason, M.D. 352 pages, 180 illustrations. $9.50. Chicago: Year Book Publishers, Inc., 1955.

The author's discussion of fractures and dislocations is extensive, appropriate, and practical.

The author emphasizes in his chapter on infections that these are less in frequency but require proper surgical principles along the lines originally set forth by Kanavel. The discussion of this problem is brief but adequate.

The author has yielded to the temptation of including in his book certain reconstructive procedures in the last two chapters on secondary tendon repairs and elective and reconstructive procedures respectively. The reader readily forgives him for this, for the chapters are brief, interesting, and worth while.

The author has performed a service of marked value in writing this book. He provides a ready reference for the surgeon handling an acute hand injury. The monograph merits a position in the library of all surgeons, who cannot and should not escape the responsibility of treating a patient with an injured hand. —*William H. Frackelton.*

THE IMPORTANCE OF THE TEXT, *Surgery of the Heart*,[3] is assured by the stature of its author, Charles P. Bailey. The mere fact that he has set down his tremendous experience with cardiovascular surgery is sufficient to recommend the book to all serious students of cardiovascular disease.

As set forth in the preface, the first purpose of the book is to present "those concepts and surgical techniques which have been developed at the Bailey Thoracic Clinic or have been proven sound in the hands of the author and his associates." The book, therefore, is to be judged on the basis of how it meets this purpose. In general, it does so admirably.

This is true, for instance, of the sections on "Surgery for Congenital Heart Disease" and on "Surgery for Acquired Heart Disease." They are extensive in their scope and in their detail. They are beautifully illustrated and contain a wealth of information. As an individual, one might disagree in certain instances with recommended operative techniques and with indications for operation. Also, one might point out that, in some instances, the results of surgery in other hands have not been the same as is implied in the text. This should not in any way detract from the value the reader attaches to these two sections of the book. They are monumental nevertheless, and they represent the mature opinion of a skilled surgeon with tremendous experience in the field. The section on "General Considerations" is extremely interesting and of real value.

All surgeons interested in treatment of heart disease by operative methods must of necessity be familiar with Bailey's book. —*John W. Kirklin.*

THE VOLUME entitled *Blood Groups in Man*[4] represents a successful attempt to compile the present knowledge and belief in regard to the classification and inheritance of the various blood groups. Because 4 years have elapsed since the first edition of this work, the present edition is very welcome. That there are two major schools in this field in respect to nomenclature and investigation is unfortunate, and that so little attempt is made to resolve their differences and to determine the true facts where their several approaches have left them in variance is deplorable, but this in no way detracts from the value of the present book to a worker in this field. This book is for established workers in the field, rather than the beginner or the clinician.

The scope of the present work has admittedly been limited by the authors as already noted, and only a very incidental attempt is made to point out the various fields of clinical application of the information presented. On the other hand, a running account of genetic applications is made, and fascinating facets of application to anthropologic research are exposed. The bibliography is not particularly biased considering that there are two major schools of endeavor in this field; there is considerable material on investigative methods, and the subject index is thoroughly adequate. —*Frank R. Elliott.*

THE SHORT, SUPERBLY ILLUSTRATED, clearly written monograph *Operative Cholangiographie*[5] concerns the diagnostic use at operation of cholangiographic and manometric methods. The work is based on findings in 261 surgical cases at the University Clinic, Basel, seen since March 1, 1950. Hess systematically discusses the information gained by these means in relationship to each of the various derangements of the biliary passages and in pancreatic disease. The techniques are described in detail. There is an inclusive introductory discussion of the anatomy and physiology of the structures concerned. Since as much stress in diagnosis is placed on the manometric readings as on the roentgenograms, the effect of drugs, anesthesia, and operative manipulation on pressures within the ducts is considered. Shortcomings and dangers of the methods are pointed out.

The 224 x-ray reproductions presented in 150 illustrations are such clear examples that the line drawings thoughtfully inserted to point up the pathologic features seem almost superfluous. The index is complete, the bibliography recent and inclusive. Although enthusiasm for the techniques presented is not now widely shared in the United States, this book contains much to interest those physicians with a knowledge of German who are concerned with the diagnosis and treatment of diseases of the biliary system, especially surgeons and radiologists. —*Elmer V. Dahl.*

ONE OF A SERIES OF HANDBOOKS of operative surgery recently published by the Year Book Publishers is *Surgery of the Small and Large Intestine*.[6] It is best

[3] SURGERY OF THE HEART. By Charles P. Bailey, M.D., M.Sc. (Med.), L.L.D. (Hon.), F.A.C.S., F.C.C.P., F.I.C.S. 1062 pages, 671 illustrations. $25.00. Philadelphia: Lea & Febiger, 1955.

[4] BLOOD GROUPS IN MAN. By R. R. Race, Ph.D. (Cambridge), M.R.C.S. (England), F.R.S., and Ruth Sanger, Ph.D. (London), B.Sc. (Sydney). 2nd ed. With a Foreword by Professor Sir Ronald Fisher, F.R.S. 400 pages, 34 illustrations. $7.50. Springfield, Ill.: Charles C Thomas, 1954.

[5] OPERATIVE CHOLANGIOGRAPHIE; TECHNIK, DIAGNOSTIK, PRAXIS. By Priv.-Doz. Dr. Walter Hess. With a foreword by Prof. Dr. R. Nissen, 201 pages, 150 illustrations. DM 42. $10.00. Stuttgart: Georg Thieme Verlag, 1955.

[6] A HANDBOOK OF OPERATIVE SURGERY; SURGERY OF THE SMALL AND LARGE INTESTINE. By Charles W. Mayo, M.D. Illustrated by Russell Drake. 340 pages, 94 illustrations. $9.00. Chicago: Year Book Publishers, Inc., 1955.

described by the opening statement of the author's preface, "The purpose of this book is to present to those interested, concise descriptions and illustrations of the more common surgical procedures performed for lesions of the small and large intestine, including the rectum."

The book admirably serves this purpose. It is both a quick reference source and teaching guide. Since a handbook serves principally the needs of students and young men in training, the author wisely presents, with very few exceptions, only techniques which are generally accepted and widely employed and avoids confusing his readers with controversial discussion of a variety of techniques. The anatomic considerations pertinent to the various lesions and surgical procedures as well as the technical steps of each operation are concisely and clearly presented in the text and abundantly illustrated in the drawings.

On occasion there may be disappointment with the failure to find descriptions of some of the uncommon lesions and surgical procedures of the bowel and anus, but as inferred by the author these were deliberately omitted for the virtue of brevity.

A valuable addition to the book are the comprehensive chapters dealing with diets, preoperative preparation, and postoperative care.

—J. Dewey Bisgard.

FOUR NEW FASCICLES of the *Atlas of Tumor Pathology*,[7] are now ready for review—"Tumors of the Soft Tissues," and "Tumors of the Stomach," by A. P. Stout, Columbia University; "Tumors of the Major Salivary Glands," by F. W. Foote, Jr. and E. L. Frazell, "Memorial Center for Cancer and Allied Diseases," and "Tumors of the Retroperitoneum, Mesentery, and Peritoneum," by L. V. Ackerman, Washington University. All are beautifully illustrated with well chosen and informative photographs of both the gross and microscopic appearances of the different tumors. The quality of the reproduction of the color photographs has improved greatly since the publication of the first fascicles. Since it is impossible in the short space available for this review to indicate the contents of these four monographs, I shall mention for each of them only a few of the features which I found especially interesting.

The two fascicles by Arthur Purdy Stout reflect to a considerable degree the accumulated wisdom and individual viewpoint of the author. His introductory remarks about the general properties of the mesenchymal tissues are most helpful and well worth repeated reading. He discusses in systematic fashion the benign and malignant tumors as well as tumor-like lesions that may be confused with the neoplasms. Stout's source material is almost exclusively from surgical patients, and there is little information about the occurrence of these interesting tumors in autopsied cases.

The same pleasing personal flavor is also apparent in Stout's fascicle on "Tumors of the Stomach." The introduction remarks about the general features of the tumors and the significance of their association with other conditions are thought provoking. The author uses a simple pathologic classification and gives a good account of the usual as well as the unusual gastric tumors.

In the fascicle on "Tumors of the Major Salivary Glands," Foote and Frazell give a thorough analysis of the pathologic material at the Memorial Center which is perhaps the largest collection in existence. As they point out much confusion exists in the literature because most reports are based upon small samples of these relatively infrequent tumors. The section on mucoepidermoid tumors is particularly fine.

Ackerman discusses retroperitoneal terms according to their probable histogenesis. He has used not only the cases from Barnes Hospital, but also those from Columbia University. The different tumors are well illustrated and their biologic behavior clearly indicated. The discussion of the pitfalls of the cytologic diagnosis of ascitic fluid is especially good.

—William B. Wartman.

IT IS INDEED STRANGE that purely descriptive gross anatomy had brought itself to a more or less static phase of development at a time when relatively nothing was known of bronchovascular arborization.

Detailed lung anatomy had been looked into rather extensively, but it required pressure from clinical surgery to stimulate interest in the grosser aspects of pulmonary structure. The fact is that clinical surgeons became the authorities in the field of pulmonary anatomy, and in his present volume entitled *Segmental Anatomy of the Lungs*,[8] Boyden assigns credit for the stimulus that led to the researches contained therein to a surgeon.

From this beginning it became apparent that only original dissections and studies would suffice, because the answer sought was not to be had in available literature. Nine years were expended collecting this information.

This book of 275 pages is beautifully bound. It is printed on excellent paper and is profusely illustrated. Many of the illustrations are colored. These are mainly semidiagrammatic charts of bronchial and vascular arborizations or both wherein color-coding aids interpretation. A very comprehensive bibliography is appended and a foreword by Evarts A. Graham pays fitting tribute to the author.

The historical evolution of the knowledge of this subject is portrayed nicely, although it seems at times that direct comparisons between the older nomenclatures (or concepts of bronchovascular relations)

[7] ATLAS OF TUMOR PATHOLOGY. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council. Section II, Fascicle 5: Tumors of the Soft Tissues. By Arthur Purdy Stout, M.D. 138 pages, 78 illustrations. $1.75. Section IV, Fascicle 11: Tumors of the Major Salivary Glands. By Frank W. Foote, Jr., M.D., and Edgar L. Frazell, M.D. 149 pages, 184 illustrations. $1.50. Section VI, Fascicle 21: Tumors of the Stomach. By Arthur Purdy Stout, M.D. 104 pages, 66 illustrations. $1.75. Section VI, Fascicles 23 and 24: Tumors of the Retroperitoneum, Mesentery, and Peritoneum. By Lauren V. Ackerman, M.D. 136 pages, 105 illustrations. Washington, D.C.: Armed Forces Institute of Pathology, 1953 and 1954.

[8] SEGMENTAL ANATOMY OF THE LUNGS; A STUDY OF THE PATTERNS OF THE SEGMENTAL BRONCHI AND RELATED PULMONARY VESSELS. By Edward A. Boyden, Ph.D. (Med. Sc.). 276 pages, 125 figures, and 12 color plates. $15.00. New York, Toronto, London: McGraw-Hill Book Co., Inc., The Blakiston Division, 1955.

and the present one are all too frequent. This makes reading somewhat repetitive and laborious if confusion is to be avoided. Nevertheless, it generally tends to give praise to the accuracy with which these more primitive studies were conducted.

The great variability in the details of the patterns of arborization are strikingly brought out and have forced the author to compile a statistical report of the frequency with which a given pattern is found. In this manner the successive chapters describe each lobe.

The embryology of the lung is discussed, particularly as it relates to the occurrence of anomalies, in a separate chapter.

The nomenclature used is essentially that devised by Jackson and Huber, the author admitting but minor deviation therefrom. Boyden's own method is used of designating artery, vein, and bronchus by the letters A., V., and B. to which a numeral is added to indicate segmental branches. Subsegmental ramifications are designated by appending further a small letter in alphabetic progression. Whereas, this method is accurate and specific it may be somewhat cumbersome to the novice.

Many of the illustrative plates have the disadvantage of being rather crowded in appearance, and therefore, tend to discourage rather than encourage perusal. Perhaps a simpler representation of such complex arborization encompassing three dimensions cannot be arranged, yet none of these features foster readability in this volume. It is, of course, true that this book was not intended to be a volume for light reading. It is, however, a record of the arborizations actually encountered in the painstaking dissection of many lungs. These are correlated with what is known about them otherwise.

Repetition of such studies may bring about alterations of interpretations or variations in what may represent prevailing patterns, but it will never detract from this as the descriptive anatomists answer to the surgeons plea for a reliable map to guide him in the dissection of segmental lung anatomy.

—Hiram T. Langston.

THE ENTHUSIASTIC ACCEPTANCE by interested physicians and physiologists of the work of Comroe and his associates as presented in *Methods in Medical Research* (1950) has prompted the preparation of an excellent monograph, especially for the medical profession, entitled *The Lung*.[9] This new publication offers, in Part 1, a more complete exposition with the addition of exceedingly good diagrams illustrating the physiologic principles for pulmonary function tests. In Part 2 there are outlined 10 clinical cases presenting different problems, each with the results of the pulmonary function studies and their interpretation with the conclusions concerning the case management. Part 3 consists of an appendix offering useful data, equations, calculations, and selected references. An additional amount of valuable information and tables are included in this new monograph.

Sections of the book are rather difficult reading for one who is not acquainted with the material presented or the scientific terminology. In Part 2 reproductions of roentgenograms of the cases described would be desirable. The advice concerning the limitations of certain pulmonary function tests and the advantages of others is helpful. However, do's and don't's are not emphasized. The book is deficient in that one still has to seek elsewhere for information regarding the technical details and equipment required for the performance of the tests.

This small volume definitely satisfies a need. It can be utilized as a medium to increase the knowledge about pulmonary physiology and function tests. Undoubtedly, it will also become a standard reference work for medical students, clinicians, and those interested in pulmonary physiology.

—Earl B. Sanborn.

IN HIS PREFACE to the publication, *Atlas Unfallchirurgischer Operationen*[10] (Atlas of Operations for Trauma) the author states: "The selection of methods has been limited to those which have proved their value in the Accident Hospital at Graz and in other Austrian Accident Hospitals. The operative technique shown in this book corresponds, on the whole, with the methods of the Professors A. Wittek, W. Ehalt, and L. Böhler. In addition operative methods developed by surgeons both in this country and in other European countries (especially in England and France) or shown in the well-known text-books of operative orthopaedics of M. Lange (Germany), Campbell and Steindler (U.S.A.) are presented in detail."

The Atlas consists of 106 quarto sized pages, 48 of which are utilized to display as many plates. Opposite each plate is a descriptive paragraph, presented in each of the three principal scientific languages: German, English, and French. The index of the plates lists the following chapters: (1) General; (2) Head and Trunk; (3) Upper Limb; (4) Lower Limb. There are 9 to 16 plates in each chapter. The first chapter illustrates such subjects as special instruments in traumatology, bone banks, skeletal traction, and tendon, nerve, and bone grafts in reconstructive surgery. Moderate use of color in the diagrams helps to clarify the illustrations and emphasize the important detail in each.

The book concludes with a 5 page bibliography, the references being largely to the work of German, British, and American authors with an occasional reference to a French or Italian contribution.

To the medical man interested in studying the foreign literature in the original the book is of interest because of the descriptive paragraphs in 3 languages which permit a comparison of the terminology used in these languages. The material is useful, therefore, to either the surgeon or the medical student who is desirous of broadening his language horizons.

—L. Margueriete Prime.

THE FIRST THIRD of the 215 pages comprising the manual entitled *Clinical Disorders of Hydration and Acid-*

[9]THE LUNG; CLINICAL PHYSIOLOGY AND PULMONARY FUNCTION TESTS. (Based on the 1954 Beaumont Lecture.) By Julius H. Comroe, Jr., M.D., Robert E. Forster, II, M.D., Arthur B. Dubois, M.D., William A. Briscoe, M.D., and Elizabeth Carlsen, A. B. 219 pages, 57 illustrations. $5.50. Chicago: The Year Book Publishers, Inc., 1955.

[10]ATLAS UNFALLCHIRURGISCHER OPERATIONEN. By Otto Russe. With a foreword by Professor Dr. Lorenz Böhler. 106 pages, 48 plates. $12.50. Wien and Bonn: Wilhelm Maudrich, 1955.

Base Equilibrium[11] is devoted to the rudiments of chemistry and renal physiology which are intended to clarify the subsequent "Clinical Considerations." In effect, although brief, the introductory material seems verbose and unlikely to capture the attention of the busy house-officer whose basic training is to be supplemented. There follows a discussion of derangements of volume and composition of fluid spaces, adrenal cortical insufficiency, diabetes insipidus, respiratory and metabolic acidosis, and acute renal insufficiency, with occasional case histories and advice concerning the management of these disorders. The bibliography is ample. Although compact and unquestionably useful, the book is surely not clearer or more inspiring than the original contributions of Gamble, Richards, Smith, and the others, of which it is a rather pedestrian digest. —*Edith B. Farnsworth.*

[11] CLINICAL DISORDERS OF HYDRATION AND ACID-BASE EQUILIBRIUM. By Louis G. Welt, M.D. 262 pages, 11 illustrations. $6.00. Boston and Toronto: Little, Brown and Co., 1955.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

EEN STUDIE VAN HET AFSLUITINGSMECHANISME TUSSEN SLOKDARM EN MAAG. By Jan Nauta. 114 pages, 21 illustrations. Leiden: H. E. Stenfert Kroese N.V., 1955.

SURGICAL PHYSIOLOGY OF THE ADRENAL CORTEX. By James D. Hardy, M.S.(Chem.), M.D., F.A.C.S. 191 pages, 34 illustrations. $5.75. Springfield, Ill.: Charles C Thomas, 1955.

CLINICAL BIOCHEMISTRY. By Abraham Cantarow, M.D., and Max Trumper, Ph.D. 5th ed. 738 pages, 54 illustrations. $9.00. Philadelphia and London: W. B. Saunders Co., 1955.

TASCHENBUCH DER PRAKTISCHEN MEDIZIN. Edited by J. Kottmaier. 3rd rev. ed. 1058 pages. DM 36. $8.60. Stuttgart: Georg Thieme Verlag, 1955.

THE EFFECT OF QUININE ON THE HUMAN UTERUS. By J. W. Jenny. 16 pages, 5 illustrations. Thesis Zürich University, 1954.

TUMORES DE TESTICULO. By Prof. Alfonso de la Peña. 115 pages, 71 illustrations. Madrid: Editorial Paz Montalvo, 1955.

NEW AND NONOFFICIAL REMEDIES, 1955. Containing Descriptions of the Articles Which Stand Accepted by the Council on Pharmacy and Chemistry of the American Medical Association on January 1, 1955. Issued under the direction and supervision of The Council on Pharmacy and Chemistry, American Medical Association. 653 pages. Philadelphia, London, Montreal: J. B. Lippincott Co., 1955.

CHIRURGIE DU CORPS THYROIDE. By Sylvain Blondin. 292 pages, 37 illustrations. 2.000 fr. Paris: Masson & Co., 1955.

CHIRURGIE DE LA RATE. By Jean Patel. 388 pages, 99 illustrations. 2.800 fr. Paris: Masson & Co., 1955.

CRISTALIZAÇÃO DO MUCO CERVICAL. By Carlos Alberto Salvatore. Tese de Doutoramento apresentada à Faculdade de Medicina da Universidade de São Paulo, Clínica Ginecológica. 127 pages, 31 illustrations. São Paulo: Faculdade de Medicina da Universidade de S. Paulo, 1955.

RADIOGRAPHIC ATLAS OF SKELETAL DEVELOPMENT OF THE KNEE. A STANDARD OF REFERENCE. By S. Idell Pyle, Ph.D., and Normand L. Hoerr, Ph.D., M.D. 82 pages, 29 plates. $4.25. Springfield, Ill.: Charles C Thomas, 1955.

ATLAS OF ROENTGEN ANATOMY OF THE SKULL. By Lewis E. Etter, B.S., M.D., F.A.C.R. With a section on The Radiographic Anatomy of the Temporal Bone by J. Brown Farrior, M.D., F.A.C.S.; and a section on The Roentgen Anatomy of the Skull in the Newborn Infant by Samuel G. Henderson, M.D., F.A.C.R., and Louise S. Sherman, B.S., M.D. 215 pages, 239 plates. $14.75. Springfield, Ill.: Charles C Thomas, 1955.

FRACTURE AND JOINT INJURIES. By Sir Reginald Watson-Jones, F.R.C.S., F.R.A.C.S.(Hon.), F.A.C.S.(Hon.), F.R.C.S.E.(Hon.), M.Ch.Orth., B.Sc., M.B., Ch.B., M.R.C.S., L.R.C.P. Vol. II. 4th ed. 1073 pages, 1613 illustrations. $22.00 (2 vols.). Baltimore: The Williams & Wilkins Co., 1955.

BIBLIOGRAPHIA MEDICA ČECHOSLOVACA. Vol. IV-1950. By Marta Procházková and Karel Ružička. 597 pages. Praha: Ústav pro zdravotnickou dokumentaci státní zdravotnické nakladatelství, 1955.

HYPOTENSION; SHOCK AND CARDIOCIRCULATORY FAILURE. By Paul G. Weil, M.D., Ph.D. 78 pages, 9 illustrations. $2.25. Philadelphia and Montreal: J. B. Lippincott Co., 1955.

PULMONARY RESECTION FOR TUBERCULOSIS. By Poul Ottosen. 166 pages, 44 illustrations. $3.00. Aarhus, Denmark: Universitetsforlaget, 1955.

THE PREVENTION OF DISEASE IN EVERYDAY PRACTICE. By Isadore Givner, B.S., M.D., F.A.C.S., and Maurice Bruger, M.Sc., M.D., C.M., F.A.C.P., and contributors. 964 pages, 50 illustrations. $20.00. St. Louis: The C. V. Mosby Co., 1955.

GRAY BOOK; ORGANIZATION, DUTIES AND REGULATIONS OF THE DIVISION. Mount Sinai Hospital of Cleveland, Division of Obstetrics and Gynecology. 2nd ed. 154 pages. $10.00. Cleveland: Mount Sinai Hospital, 1955.

THE POSTURAL COMPLEX; OBSERVATIONS AS TO CAUSES, DIAGNOSIS AND TREATMENT. By Laurence Jones, B.S., M.D. 156 pages, 78 illustrations. $9.75. Springfield, Ill.: Charles C Thomas, 1955.

THE JOSIAH MACY, JR. FOUNDATION, 1930–1955; A REVIEW OF ACTIVITIES. 174 pages. New York: The Josiah Macy, Jr. Foundation, 1955.

A HANDBOOK OF OPERATIVE SURGERY; SURGERY OF THE STOMACH AND DUODENUM. By Claude E. Welch, M.D., D.Sc.(hon.). 2nd rev. ed. Illustrated by Muriel McLatchie Miller. 370 pages, 79 plates. $9.00. Chicago: Year Book Publishers, Inc., 1955.

SEXUAL PRECOCITY. By Hugh Jolly, M.A., M.D.(Camb.), M.R.C.P. 276 pages, 69 illustrations. $6.75. Springfield, Ill.: Charles C Thomas, 1955.

THE BODY FLUIDS; BASIC PHYSIOLOGY AND PRACTICAL THERAPEUTICS. By J. Russell Elkinton, M.D., and T. S. Danowski, M.D. 626 pages, illustrated. $10.00. Baltimore: The Williams & Wilkins Co., 1955.

GYNECOLOGY; SURGICAL TECHNIQUES. Compiled and edited by Robert J. Lowrie, M.A., M.D., F.A.C.S., D-OG. Foreword by J. P. Greenhill, M.D. 523 pages, illustrated. $17.75. Springfield, Ill. Charles C Thomas, 1955.

AMERICAN COLLEGE OF SURGEONS

ALFRED BLALOCK, Baltimore, *President*
WARREN H. COLE, Chicago, *President-Elect*

PRELIMINARY PLANS FOR THE 41st CLINICAL CONGRESS THE CONRAD HILTON HOTEL, CHICAGO, ILLINOIS OCTOBER 31 TO NOVEMBER 4, 1955

THE HISTORY of these world-famous Clinical Congresses dates back to 1910, and to the city of Chicago. In February 1910, Dr. Franklin H. Martin, later founder of the American College of Surgeons, invited the 3,000 physicians who made up the subscription list of SURGERY, GYNECOLOGY & OBSTETRICS, which he had originated in 1905, to come to Chicago to observe the work of the leading surgeons of this city.

The gathering was such a success that those in attendance expressed a desire to perpetuate such meetings, and a permanent organization for this purpose, known as the Clinical Congress of Surgeons of North America, was formed in November 1910.

In succeeding Clinical Congresses the character and high aims of the future American College of Surgeons began to take form and in May 1913, the College was founded. Just a few months later, in November 1913, the first Convocation was held in Chicago, with 1,059 candidates admitted to fellowship. The Clinical Congress of Surgeons of North America was continued until 1917, when it was merged with the College.

Development of the program for the Congress has come a long way since its inception in 1910 and, since postgraduate education of the surgeon is a never-ending College ideal, the scope of the Congress program is widened each year. Now the Congress is renowned as probably the most widely instructive meeting of surgeons in the world.

Headquarters for the meetings and exhibits will be the Conrad Hilton Hotel, Chicago's largest hotel, located on famous Michigan Boulevard. Some sessions will be held in nearby Blackstone Theatre, Congress Hotel, Eighth Street Theatre, and Eleventh Street Theatre.

Postgraduate Courses

Eight postgraduate courses will be given this year, in the mornings from 8:30 to 11:30 sharp. All courses meet Monday through Thursday, with the exception of Gynecology and Obstetrics, which meets Monday through Friday. Registration for these invaluable courses is limited, so that it is advisable to make advance reservations. Registration forms may be obtained from The American College of Surgeons, 40 East Erie Street, Chicago 11, Illinois. Fee is $5.00 per course. Courses are progressive, so that one can register for one course only. The program appears on the following pages.

Evening Sessions

On Monday evening, designated as the President's Evening, Dr. Alfred Blalock, President, will preside over the program, at which Dr. J. Garrott Allen, Chairman of the Chicago Advisory Committee on Arrangements, will give the Address of Welcome, Dr. I. S. Ravdin, Chairman, Board of Regents, will introduce the guests, and the distinguished President of Columbia University, Grayson Kirk, will give the Tenth Martin Memorial Lecture.

On Friday evening, the Convocation evening, new Fellows will be received into the College, Honorary Fellowships conferred, and the address of the new President, Dr. Warren H. Cole, will be heard. Dr. Cole will speak on "Surgical Philosophy Old and New."

Color Television

An outstanding color television program is assured this year. Surgical procedures performed at Illinois Research and Educational Hospitals will be viewed in the Conrad Hilton Hotel, with this innovation: spectators may relay questions to the operating room at Illinois Research. A panel of two or three teachers, in addition to the surgeon whose work is being shown, will discuss the problems presented by the operation and answer questions put by the viewers.

Smith, Kline & French Laboratories, Philadelphia, are sponsors of color television for the Clinical Congress. Dr. J. Garrott Allen, the College's national chairman for television, and Dr. Warren H. Cole, head of the Department of Surgery at the University of Illinois College of Medicine, are in charge of the program, assisted by Dr. John T. Reynolds.

The television program may be viewed each morning from 9:00 a.m. to 12:00 noon. Schedule of operations will be published in the *Daily Bulletin* of the Clinical Congress.

Ciné Clinic

Ciné clinics are scheduled for viewing Tuesday through Friday mornings, 8:30 to 12:30 p.m. This year's program will not be restricted to films made only by surgeons in the geographic area of Chicago, but rather to films made by surgeons throughout the United States. A special feature will be the panel on cancer of the large intestine on Tuesday morning, including panelists Owen H. Wangensteen, Warren H. Cole, Leon Goldman, and Walter G. Maddock.

Davis & Geck, Inc., Danbury, Connecticut, are sponsors of the Ciné Clinic program.

A general outline of the program follows:

Hindquarter Amputation. BRADLEY L. COLEY, New York.
Mediastinal Tumors. JOHN H. GIBBON, Philadelphia.
Cardiac Surgery. WILLIS J. POTTS, Chicago.
Radical Surgery for Oral Cancer. DANELY P. SLAUGHTER, Chicago.
Surgery for Massive Ulcer of the Leg. CARL A. MOYER, St. Louis.
Transthoracic Gastrectomy. RICHARD H. SWEET, Boston.
Varicose Veins. GEZA DE TAKATS, Chicago.
Surgery of the Thyroid. GEORGE W. CRILE, JR. Cleveland.
A Phase of Plastic Surgery. JAMES BARRETT BROWN, St. Louis.

Dr. Hilger Perry Jenkins, Chairman, and his Medical Motion Picture Committee are in charge of all films shown during the Congress.

Medical Motion Pictures

Medical motion pictures will be shown mornings and afternoons each day, with the tentative plan of showing films devoted to the specialties during the mornings, and to general surgery during the afternoons. On Monday, general surgery will be featured all day.

"New and Unusual Problems in Surgery" is the title of the Motion Picture Symposium scheduled for Wednesday evening from 7:30 to 10:00 p.m. Each film shown on this program will be narrated by the author in person. The program appears on the following pages.

The entire program will be listed in detail in the official Program of the Congress, and the *Daily Bulletin* issued during the five day meeting.

Forum on Fundamental Surgical Problems

There will be 16 Surgical Forum sessions this year, running mornings and afternoons, Monday through Friday. A total of 177 papers will be heard in all, including the reports in the surgical specialties.

"What's New In Surgery?" initiated with such great success at the 1954 Congress will be given again this year, as part of the general session on Friday morning. Dr. Harris B. Shumacker Jr. is Forum Chairman. Authors and papers are listed on following pages.

Ophthalmology and Otolaryngology

No Ophthalmology or Otolaryngology sessions will be held this year due to the fact that the meeting of the American Academy of Ophthalmology and Otolaryngology will be held in Chicago this year immediately preceding the Congress.

Advance Reservations

All official registration forms—advance registration, postgraduate courses, transportation, and hotel accommodations—must be obtained

from The American College of Surgeons, 40 East Erie Street, Chicago 11, Illinois.

By advance planning you avoid any waiting in line, for you are handed your badge immediately on checking in at the Advance Registration Desk, and your postgraduate course ticket has already been mailed to you. Also, you are more likely to obtain your first choice in the course you wish and in other accommodations.

The official Registration Desks will observe the following hours: Sunday, October 30, 3 p.m. to 7:30 p.m.; Monday, October 31, 8 a.m. to 6 p.m.; and Tuesday through Friday, November 1 to 4, 8 a.m. to 5 p.m.

Fees, except for the $5.00 fee for the Postgraduate Courses, are not required of Initiates, Endorsed Junior Candidates, or Surgical Residents. Fellows whose dues are paid to December 31, 1954, do not pay any registration fee; those whose dues are not paid are charged $20.00. Non-Fellows pay $20.00, and members of the Federal Services $10.00.

PROGRAM IN BRIEF

Monday, October 31, 1955

8:30–11:30 Postgraduate Courses:
- Cardiovascular Surgery
- Preoperative and Postoperative Care
- Gastrointestinal Tract
- Diseases of the Liver, Biliary Tract, and Pancreas
- Obstetric and Gynecologic Surgical Care
- Neoplasms of the Musculoskeletal System; Diagnosis, Treatment, and Prognosis
- Surgical Aspects of Pulmonary Disease
- Surgery of the Hand

8:30–12:00 Medical Motion Pictures
9:00–12:00 Forum: Heart and Great Vessels
9:00–12:00 Forum: Infections and Burns
9:00–12:00 Television
10:00–12:00 Panel Discussion: Thyroid
1:30– 3:00 Clinicopathology Conference
1:30– 3:00 Panel: Obstetrics and Gynecology
1:30– 5:00 Medical Motion Pictures
2:00– 5:00 Television
2:00– 5:00 Forum: Gastrointestinal Tract
2:00– 5:00 Forum: Plastic Surgery
2:00– 5:00 Forum: Urology
3:30– 5:00 Panel: Obstetrics and Gynecology
3:30– 5:00 Panel: Parenteral Therapy
8:30–10:00 President's Evening

Tuesday, November 1

8:30–10:00 Postgraduate Courses: Same as Monday
8:30–12:00 Medical Motion Pictures
8:30–12:00 Ciné Clinic
9:00–12:00 Television
9:00–12:00 Forum: Heart and Great Vessels
9:00–12:00 Forum: Metabolism and Nutrition
1:30– 3:00 Panel: Urology
1:30– 3:00 Panel: Obstetrics and Gynecology
1:30– 3:00 Panel: Carcinoma of the Breast
1:30– 5:00 Medical Motion Pictures
2:00– 5:00 Television
2:00– 5:00 Symposium on Trauma
2:00– 5:00 Forum: Liver, Biliary Tract, and Pancreas
3:30– 5:00 Panel: Surgery in Cardiac Disease
3:30– 5:00 Panel: Obstetrics and Gynecology

Wednesday, November 2

8:30–11:30 Postgraduate Courses: Same as Monday
8:30–12:00 Medical Motion Pictures
8:30–12:30 Ciné Clinic
9:00–12:00 Television
9:00–12:00 Forums
1:30– 3:00 Panel: Surgery and Anesthesia
1:30– 3:00 Panel: Obstetrics and Gynecology
1:30– 3:00 Medical Motion Pictures
2:00– 5:00 Television
2:00– 5:00 Symposium on Cancer
2:00– 5:00 Forums
3:30– 5:00 Panel: Benign Lesions of Pancreas
3:30– 5:00 Panel: Urology
3:30– 5:00 Panel: Obstetrics and Gynecology
7:30–10:00 Motion Picture Symposium

Thursday, November 3

8:30–11:30 Postgraduate Courses: Same as Monday
8:30–12:00 Medical Motion Pictures
8:30–12:30 Ciné Clinic
9:00–12:00 Television
9:00–12:00 Symposium: Neurosurgery
9:00–12:00 Forums
1:30– 3:00 Panel: Urology
1:30– 3:00 Panel: Surgery of the Colon
1:30– 3:00 Forum: Obstetrics and Gynecology
1:30– 3:00 Symposium on Graduate Training
1:30– 3:00 Medical Motion Pictures
2:00– 5:00 Television
3:15– 3:45 Trauma Oration
4:00– 5:30 Annual Meeting of Fellows

Friday, November 4

8:30–11:30 Postgraduate Course
8:30–12:00 Medical Motion Pictures
8:30–12:30 Ciné Clinic
9:00–10:30 Panel: Orthopedic Surgery
9:00–12:00 Forum Summary
9:00–12:00 Television
9:00–12:00 Forum: Neurosurgery
1:30– 4:45 Panel Discussions
2:00– 5:00 Television
8:30–10:00 Convocation

PRELIMINARY PROGRAM

Evening Sessions

PRESIDENT'S EVENING

Monday, 8:30—10:00 p.m., Grand Ballroom, The Conrad Hilton

ALFRED BLALOCK, M.D., F.A.C.S., Baltimore; President, American College of Surgeons, *Presiding*.

Address of Welcome. J. GARROTT ALLEN, M.D., F.A.C.S., Chicago; Chairman, Chicago Advisory Committee on Arrangements.

Introduction of Guests. I. S. RAVDIN, M.D., F.A.C.S., Philadelphia; Chairman, Board of Regents.

The Tenth Martin Memorial Lecture: Current Dilemmas for Doctors and Others. GRAYSON KIRK, New York; President, Columbia University.

CONVOCATION

Friday, 8:30—10:00 p.m., Grand Ballroom, The Conrad Hilton

ALFRED BLALOCK, M.D., F.A.C.S.; President, *Presiding*.

Procession. Initiates, Governors, Officers, Regents, and Guests.

Invocation.

Presentation of Initiates and Conferring of Fellowships.

Conferring of Honorary Fellowships.

Installation of New Officers:

Second Vice President: DERRICK VAIL, M.D., F.A.C.S., Chicago.

First Vice President: W. EMORY BURNETT, M.D., F.A.C.S., Philadelphia.

President: WARREN H. COLE, M.D., F.A.C.S., Chicago.

Address of the President: Surgical Philosophy Old and New. WARREN H. COLE, M.D., F.A.C.S.

Recession.

Annual Meeting — Board of Governors

Sunday, 9:00 a.m.—5:00 p.m. (with Luncheon), Astoria Ballroom, The Conrad Hilton

WILLARD H. PARSONS, M.D., F.A.C.S., Vicksburg; Chairman, Board of Governors, *Presiding*.

Minutes of the 1954 Annual Meeting of the Board of Governors. HOWARD H. BRADSHAW, M.D., F.A.C.S., Winston-Salem; Secretary, Board of Governors.

Report of the Chairman—Resume of Interim Activities. WILLARD H. PARSONS, M.D., F.A.C.S.

Report of the Executive Committee. HOWARD H. BRADSHAW, M.D., F.A.C.S.

Report of the President, ALFRED BLALOCK, M.D., F.A.C.S., Baltimore.

Report of the Chairman, Board of Regents. I. S. RAVDIN, M.D., F.A.C.S., Philadelphia.

Report of the Director. PAUL R. HAWLEY, M.D., F.A.C.S., Chicago.

Report of Committee to Study the Junior Candidate Group. CARL A. MOYER, M.D., F.A.C.S., St. Louis, Chairman.

Report of Committee to Study the Bylaws of the College. CHARLES C. HIGGINS, M.D., F.A.C.S., Cleveland, Chairman.

Report of Committee to Study the Problem of Total Number of Governors of the College and of their Distribution. DERYL HART, M.D., F.A.C.S., Durham, Chairman.

Report of Committee to Study Itinerant Surgery and Surgeons. GEORGE W. WALDRON, M.D., F.A.C.S., Houston, Chairman.

Report of Committee to Study the College Cancer Program. JOHN C. BURCH, M.D., F.A.C.S., Nashville, Chairman.

Report of Committee to Study the Procedures on Inspection of Hospitals for Accreditation and of the Effectiveness of the Credentials Committees. WALTER C. JONES, JR., M.D., F.A.C.S., Miami, Chairman.

Report of the Committee to Study the Advisability of Requiring Candidates for Fellowship in the College to Submit Photostatic Copies of Their Records. GEORGE H. HUNT, M.D., F.A.C.S., Washington, D. C., Chairman

Individual Resolutions by Governors.

Announcements.

ADJOURNED MEETING—BOARD OF GOVERNORS

Thursday, 3:30—3:45 p.m., West Ballroom, The Conrad Hilton

WILLARD H. PARSONS, M.D., F.A.C.S., Chairman; *Presiding*.

Report of Committee on Nominations to the Board of Governors.

Report of Nominating Committee on Election of Regents.

Election of Regents of College.
Report of Nominating Committee on Election of Officers, Board of Governors.
Election of Officers, Board of Governors.
Announcement of Nominating Committee, Board of Governors 1955–1956.
Adjournment.

Annual Meeting of Fellows

Thursday, 4:00—5:30 p.m., Grand Ballroom, The Conrad Hilton

ALFRED BLALOCK, M.D., F.A.C.S.; President, *Presiding*.
Call to Order by the President.
Election of Officers of the College.
Election of Governors of the College.
Deliberations of the Board of Governors—1955 Annual Meeting
Report of the Treasurer.
Reports of Standing Committees:
- Cancer
- Trauma
- Graduate Training
- Medical Motion Pictures
- Nutrition of the Surgical Patient
- Blood Transfusions and Allied Problems

Reports of Departments, Summary by The Director.
Resolution Re Amendment of Articles of Incorporation.
Adjournment.

General Sessions

Monday, 10:00 a.m.—12:00 noon, Grand Ballroom

SURGERY OF THE THYROID

Moderator: RICHARD B. CATTELL, M.D., F.A.C.S., Boston.
Collaborators: THOMAS J. ANGLEM, M.D., F.A.C.S., Brookline, Mass.; B. MARDEN BLACK, M.D., F.A.C.S., Rochester, Minn.; HOWARD A. PATTERSON, M.D., F.A.C.S., New York.

1:30—3:00 p.m., Grand Ballroom

CLINICOPATHOLOGY CONFERENCE

Moderator: EDWIN F. HIRSCH, M.D., F.A.C.P., Chicago.
Collaborators: To be announced.

3:30—5:00 p.m., Grand Ballroom

PARENTERAL THERAPY

Moderator: CARL A. MOYER, M.D., F.A.C.S., St. Louis, Mo.
Collaborators: WILLIAM E. ABBOTT, M.D., F.A.C.S., Cleveland; HALVOR N. CHRISTENSEN, PH.D., Ann Arbor; DAVID V. HABIF, M.D., F.A.C.S., New York.

Tuesday, 1:30—3:00 p.m., Grand Ballroom

CARCINOMA OF THE BREAST

Moderator: CLARENCE E. GARDNER, JR., M.D., F.A.C.S., Durham.
Collaborators: SIR STANFORD CADE, M.D., F.R.C.S., London, England; HERBERT WILLY MEYER, M.D., F.A.C.S., Rancho Santa Fe, Calif.; THOMAS G. ORR, SR., M.D., F.A.C.S., Kansas City, Kansas; HENRY THOMAS RANDALL, M.D., F.A.C.S., New York.

3:30—5:00 p.m., Grand Ballroom

SURGERY IN PATIENTS WITH CARDIAC DISEASE

Moderator: CHARLES G. JOHNSTON, M.D., F.A.C.S., Detroit.
Collaborators: WRIGHT R. ADAMS, M.D., F.A.C.P., Chicago; STUART C. CULLEN, M.D., Iowa City; RUDOLF J. NOER, M.D., F.A.C.S., Louisville.

Wednesday, 1:30—3:00 p.m., Grand Ballroom

SURGERY AND ANESTHESIA

Moderator: FRANK GERBODE, M.D., F.A.C.S., San Francisco.
Collaborators: FRANK F. ALLBRITTEN, JR., M.D., F.A.C.S., Kansas City, Kansas; STUART C. CULLEN, M.D., Iowa City; PAUL R. DUMKE, M.D., Detroit; FRANCIS D. MOORE, M.D., F.A.C.S., Boston.

3:30—5:00 p.m., Grand Ballroom

BENIGN LESIONS OF THE PANCREAS

Moderator: JOHN H. MULHOLLAND, M.D., F.A.C.S., New York.

Collaborators: HENRY DOUBILET, M.D., F.A.C.S., New York; PHILIP F. PARTINGTON, M.D., F.A.C.S., Cleveland, KENNETH W. WARREN, M.D., F.A.C.S., Boston.

Thursday, 1:30—3:00 p.m., Grand Ballroom

SURGERY OF THE COLON

Moderator: CLAUDE F. DIXON, M.D., F.A.C.S., Rochester, Minn.

Collaborators: A. STEPHENS GRAHAM, M.D., F.A.C.S., Richmond; JESSIE C. GRAY, M.D., F.A.C.S., Toronto; THOMAS M. MILLAR, M.B., F.R.C.S. (E), Edinburgh, Scotland.

Friday, 9:00 a.m.—12 noon, Grand Ballroom

What's New In Surgery? (Forum Summary). HARRIS B. SHUMACKER, JR., M.D., F.A.C.S., Indianapolis, *Chairman.*

Surgical Specialties

UROLOGY

Tuesday, 1:30—3:00 p.m., South Ballroom

MANAGEMENT OF UNDESCENDED TESTES

Moderator: NORRIS J. HECKEL, M.D., F.A.C.S., Chicago.

Collaborators: ROBERT J. PRENTISS, M.D., F.A.C.S., San Diego; JOHN N. ROBINSON, M.D., F.A.C.S., New York; LESLIE B. AREY, PH.D., SC.D., Chicago; ORMOND S. CULP, M.D., F.A.C.S., Rochester, Minn.

Wednesday, 3:30—5:00 p.m., South Ballroom

MANAGEMENT OF PROSTATIC HYPERTROPHY

Moderator: VICTOR F. MARSHALL, M.D., F.A.C.S., New York.

Collaborators: JAMES M. CAMPBELL, M.D., F.A.C.S., Saskatoon; CHARLES D. CREEVY, M.D., Minneapolis; ROBERT LICH, JR., M.D., F.A.C.S., Louisville; SAMUEL A. VEST, M.D., F.A.C.S., Charlottesville.

Thursday, 1:30—3:00 p.m., South Ballroom

MANAGEMENT OF RENAL LITHIASIS

Moderator: CHARLES C. HIGGINS, M.D., F.A.C.S., Cleveland.

Collaborators: WILLARD E. GOODWIN, M.D., F.A.C.S., Los Angeles; EDWIN L. PRIEN, M.D., F.A.C.S., Brookline, Mass.; EPHRAIM SHORR, M.D., New York; HARRY M. SPENCE, M.D., F.A.C.S., Dallas; WILLIAM L. VALK, M.D., F.A.C.S., Kansas City, Kan.

Friday, 1:30—3:00 p.m., South Ballroom

EVALUATION OF SUPRARADICAL SURGERY IN MALIGNANT DISEASE OF LOWER ABDOMEN AND PELVIS

Moderator: EUGENE M. BRICKER, M.D., F.A.C.S., St. Louis, Missouri.

Collaborators: General Surgery—R. KENNEDY GILCHRIST, M.D., F.A.C.S., Chicago; Radiology—JAMES J. NICKSON, M.D., New York; Gynecology—HOWARD ULFELDER, M.D., F.A.C.S., Boston; Urology—RUBEN H. FLOCKS, M.D., F.A.C.S., Iowa City.

GYNECOLOGY AND OBSTETRICS

Monday, 1:30—3:00 p.m., Gold Room, Congress Hotel

THE PLACE OF THE "D & C" IN GYNECOLOGY

Moderator: LEWIS C. SCHEFFEY, M.D., F.A.C.S., Philadelphia.

Collaborators: ROGER B. SCOTT, M.D., Cleveland; E. LAWRENCE HECHT, M.D., F.A.C.S., New York; JOSEPH ANDREW HEPP, M.D., F.A.C.S., Pittsburgh.

3:30—5:00 p.m.

CESAREAN SECTION

Moderator: CURTIS TYRONE, M.D., F.A.C.S., New Orleans.

Collaborators: A. CHARLES POSNER, M.D., F.A.C.S., New York; H. HUDNALL WARE, JR., M.D., F.A.C.S., Richmond; EDWARD G. WATERS, M.D., F.A.C.S., Jersey City.

Tuesday, 1:30—3:00 p.m., Gold Room, Congress Hotel

CONSERVATION OF OVARIAN TISSUE

Moderator: JOHN MCLEAN MORRIS, M.D., New Haven.

Collaborators: CLYDE L. RANDALL, M.D., Buffalo; JOHN ARTHUR STALLWORTHY, M.B., CH.B., F.R.C.S., Oxford, England.

3:30—5:00 p.m.

ESTIMATION OF PELVIC SIZE

Moderator: M. EDWARD DAVIS, M.D., F.A.C.S., Chicago.

Collaborators: PAUL C. HODGES, M.D., Chicago; WILLIAM F. MENGERT, M.D., Chicago; CHARLES M. STEER, M.D., F.A.C.S., New York.

Wednesday, 1:30—3:00 p.m., Gold Room, Congress Hotel

BLOOD CLOTTING PROBLEMS IN OBSTETRICS

Moderator: DUNCAN E. REID, M.D., Boston.

Collaborators: C. PAUL HODGKINSON, M.D., F.A.C.S., Detroit; WILLIAM CURRY MOLONEY, M.D., F.A.C.P., Boston; DANIEL J. MULLANE, M.D., F.A.C.S., Brookline.

3:30—5:00 p.m.

STUDIES IN THE RADIOSENSITIVITY OF TUMORS

Moderator: S. B. GUSBERG, M.D., F.A.C.S., New York.

Collaborators: JOHN B. GRAHAM, M.D., F.A.C.S., Boston; FRANKLIN L. PAYNE, M.D., F.A.C.S., Philadelphia; JAMES W. REAGAN, M.D., Cleveland.

Thursday, 1:30—3:00 p.m., Gold Room, Congress Hotel

Surgical Forum Reports in Gynecology and Obstetrics

Friday, 1:30—3:00 p.m., Gold Room, Congress Hotel

HAZARDS OF FETAL EXISTENCE

Moderator: JOHN PARKS, M.D., F.A.C.S., Washington.

Collaborators: T. N. EVANS, M.D., F.A.C.S., Ann Arbor; ARTHUR B. HUNT, M.D., Rochester, Minn.; J. JACKSON STODDARD, M.D., Milwaukee.

3:15—5:00 p.m.

CARE OF PATIENT UNDER RADIATION THERAPY

Moderator: HERBERT E. SCHMITZ, M.D., F.A.C.S., Chicago.

Collaborators: LANGDON PARSONS, M.D., F.A.C.S., Boston; FRANK R. SMITH, M.D., F.A.C.S., New York; HENRY L. SCHMITZ, M.D., Chicago.

NEUROLOGIC SURGERY

Thursday, 9:00—10:30 a.m., Normandy Lounge

THE MANAGEMENT OF FACIAL PAIN, Symposium.

Chairman: BRONSON S. RAY, M.D., F.A.C.S., New York.

Participants: Surgical Treatment of Tic Douloureux (Including Glossopharyngeal Neuralgia and Exclusive of Injections and Medical Treatment)—GEORGE S. BAKER, M.D., F.A.C.S., Rochester, Minn.

Nonsurgical Treatment of Tic Douloureux (Including Injection Methods and Medical Therapy)—GUY L. ODOM, M.D., Durham.

Atypical Facial Neuralgia and Allied Facial Pain—HARRY WILKINS, M.D., F.A.C.S., Oklahoma City.

10:35 a.m.—12:00 noon

THE SURGICAL MANAGEMENT OF UPPER EXTREMITY PAIN DUE TO CERVICAL DISC

Chairman: E. S. GURDJIAN, M.D., F.A.C.S., Detroit.

Participants: Surgical Management of Upper Extremity Pain Due to Cervical Disc—FRANCIS ASBURY ECHLIN, M.D., F.A.C.S., New York.

Surgical Management of Upper Extremity Pain Due to Anterior Scalene and Cervical Rib Syndrome—JOHN RAAF, M.D., F.A.C.S., Portland, Oregon.

Upper Extremity Pain Due to Other Causes—FRANK H. MAYFIELD, M.D., F.A.C.S., Cincinnati.

Friday, 9:00 a.m.—12:00 noon, Normandy Lounge

NEUROSURGICAL SESSION OF THE SURGICAL FORUM

C. HUNTER SHELDEN, M.D., F.A.C.S., Pasadena, *Presiding.*

Twelve papers will present results of recent research in the field of Neurologic Surgery.

Friday, 1:30—4:45 p.m., Normandy Lounge

SYMPOSIUM

EDGAR F. FINCHER, M.D., F.A.C.S., Emory University, *Presiding.*

Present-Day Evaluation of Hypothermia in Neurosurgery. E. HARRY BOTTERELL, M.D., F.R.C.S.(C), Toronto.

Present-Day Evaluation of Cordotomy. EDGAR A. KAHN, M.D., F.A.C.S., Ann Arbor.

An Evaluation of Present-Day Management of Hydrocephalus. DONALD D. MATSON, M.D., F.A.C.S., Boston.

An Evaluation of Present-Day Management of Involuntary Movements. A. EARL WALKER, M.D., F.A.C.S., Baltimore.

ORTHOPEDIC SURGERY

Friday, 9:00—10:30 a.m., Eleventh Street Theatre

FRACTURES OF THE LOWER END OF THE RADIUS AND OF THE CARPAL BONES

Moderator: JESSE T. NICHOLSON, M.D., F.A.C.S., Philadelphia.

Collaborators: C. FRED FERCIOT, M.D., F.A.C.S., Lincoln, Neb.; HARRISON L. MCLAUGHLIN, M.D., F.A.C.S., New York; RALPH SOTO-HALL, M.D., F.A.C.S., San Francisco; PAUL B. STEELE, M.D., F.A.C.S., Pittsburgh.

1:30—4:45 p.m.

DIFFERENTIAL DIAGNOSIS AND TREATMENT OF NECK, SHOULDER AND ARM PAIN

Moderator: JOSEPH A. FREIBERG, M.D., F.A.C.S., Cincinnati.

Collaborators: FRANK H. MAYFIELD, M.D., F.A.C.S., Cincinnati; WILLIAM BEECHER SCOVILLE, M.D., F.A.C.S., Hartford; HAROLD A. SOFIELD, M.D., F.A.C.S., Oak Park, Ill.; FRANK P. WALSH, M.D., F.A.C.S., Detroit.

PLASTIC SURGERY

Friday, 1:30—4:45 p.m., Florentine Room, Congress

EXPERIENCES IN TISSUE BANKING AND PROBLEMS OF TISSUE TRANSPLANTATION

Moderator: GEORGE W. HYATT, Lt. Commander (M.C.), U.S.N., Bethesda.

Collaborators: GLENN H. ALGIRE, M.D., Bethesda; MINOT P. FRYER, M.D., F.A.C.S., St. Louis; JOHN W. SAVILLE, Lt. (M.C.), U.S.N., Bethesda.

3:15—4:45 p.m.

CARCINOMA OF THE FACE, MOUTH, JAW AND NECK

Moderator: WILLIAM F. MACFEE, M.D., F.A.C.S., New York.

Collaborators: TRUMAN G. BLOCKER, JR., M.D., F.A.C.S., Galveston; JOSEPH E. MURRAY, M.D., F.A.C.S., Boston; LOUIS T. BYARS, M.D., F.A.C.S., St. Louis.

THORACIC SURGERY

Friday, 1:30—3:00 p.m., Waldorf Ballroom

SURGICAL MANAGEMENT OF "CYSTIC" DISEASES OF THE LUNG AND SPONTANEOUS PNEUMOTHORAX

Moderator: LYMAN A. BREWER III, M.D., F.A.C.S., Los Angeles.

Collaborators: O. THERON CLAGETT, M.D., F.A.C.S., Rochester, Minn.; FREDERICK G. KERGIN, M.D., Toronto; RICHARD H. SWEET, M.D., F.A.C.S., Boston; ROBERT H. WYLIE, M.D., F.A.C.S., New York.

3:15—4:45 p.m.

RECENT DEVELOPMENTS IN CARDIAC SURGERY

Moderator: WILLIS J. POTTS, M.D., F.A.C.S., Chicago.

Collaborators: HENRY T. BAHNSON, M.D., F.A.C.S., Baltimore; CONRAD R. LAM, M.D., F.A.C.S., Detroit; C. WALTON LILLEHEI, M.D., F.A.C.S., Minneapolis.

Postgraduate Courses

PREOPERATIVE AND POSTOPERATIVE CARE

HENRY N. HARKINS, M.D., F.A.C.S., Seattle, *Chairman.*

Monday, 8:30—11:30 a.m., , West Ballroom

APPLIED METABOLISM IN SURGICAL CARE. I. BASIC PHYSIOLOGY.

FRANCIS D. MOORE, M.D., F.A.C.S., Boston, *Moderator.*

Patterns of Autonomic Activity in Wounding and Shock. F. A. SIMEONE, M.D., F.A.C.S., Cleveland.

Patterns of Response to Anesthetic Agents in Relation to Shock and Hypotension. LEROY D. VANDAM, M.D. Boston.
The Blood Volume; Relation to Whole Body Hematocrit and Other Fluid Compartments. FRANCIS D. MOORE, M.D., F.A.C.S., Boston.
Neuroendocrine Activity in Stress, Trauma, and Surgery. DAVID M. HUME, M.D., F.A.C.S., Boston.
The Effect of Trauma on Metabolism of Water and Electrolyte. WILLIAM D. HOLDEN, M.D., F.A.C.S., Cleveland.
Studies on Renal Function and Renal Hemodynamics in Surgical Patients. BOYD W. HAYNES, JR., M.D., F.A.C.S., Richmond, Virginia.
The Normal Regulation of Acid-Base Balance. DAVID V. HABIF, M.D., F.A.C.S., New York.
Calories, Nitrogen and Vitamins in the Diet. STANLEY M. LEVENSON, M.D., Washington, D. C.

Tuesday, 8:30—11:30 a.m., West Ballroom

APPLIED METABOLISM IN SURGICAL CARE. II. THERAPY.
FRANCIS D. MOORE, M.D., F.A.C.S., Boston, *Moderator.*
Whole Blood Dextran and the Plasma Volume Extenders in Shock. JONATHAN E. RHOADS, M.D., F.A.C.S., Philadelphia.
The Resuscitation of the Severely Injured Patient for Surgery. JOHN M. HOWARD, M.D., Houston.
The Management of Extrarenal Losses of Water and Electrolyte. WILLIAM E. ABBOTT, M.D., F.A.C.S., Cleveland.
Special Problems in the Early Burn. CURTIS P. ARTZ, Lt. Col., (M.C.), U.S.A., F.A.C.S., Fort Sam Houston.
The Treatment of Acidosis, Alkalosis, and Hypokaliemia. HENRY T. RANDALL, M.D., F.A.C.S., New York.
The Early Recognition and Management of Renal Failure. PAUL E. TESCHAN, Major, (M.C.), U.S.A., Fort Sam Houston.
The Nature of Surgical Depletion. JAMES D. MCMURREY, M.D., Boston.
Some Common Myths and Fables of Surgical Care. FRANCIS D. MOORE, M.D., F.A.C.S., Boston.

Wednesday, 8:30—11:30 a.m., West Ballroom

J. GARROTT ALLEN, M.D., F.A.C.S., Chicago, *Moderator.*
The Preparation of the Patient in Shock for Surgical Operation. WILLIAM T. FITTS, JR., M.D., F.A.C.S., Philadelphia.
Current Status of the Amino-Acid Hydrolysates. WILLIAM D. HOLDEN, M.D., F.A.C.S., Cleveland.
Certain Aspects of Medical Care in Surgical Patients. JOSEPH B. KIRSNER, M.D., F.A.C.P., Chicago.
Preoperative and Postoperative Considerations in the Management of the Surgical Patient Suffering from Massive Bleeding in the Upper Gastrointestinal Tract. CHARLES F. W. ILLINGWORTH, M.D., CH.M., F.R.C.S. (Edin.), F.R.F.P.S. (Glas.), F.A.C.S., Glasgow.

Thursday, 8:30—11:30 a.m., West Ballroom

BACTERIAL FACTORS IN ANTIBIOTICS IN PREOPERATIVE AND POSTOPERATIVE CARE
PHILIP B. PRICE, M.D., F.A.C.S., Salt Lake City, *Moderator.*
Choice of Antibiotics in Surgical Infections; Optimum Methods of Use. EDWIN J. PULASKI, Lt. Col., (M.C.), U.S.A., F.A.C.S., Honolulu.
The Newer Antibiotics; Recommendations and Warnings. WILLIAM A. ALTEMEIER, M.D., F.A.C.S., Cincinnati.
The Operation as a Bacteriological Hazard. CARL W. WALTER, M.D., F.A.C.S., Boston.
Bacterial Peritonitis; Prevention and Treatment. EDGAR J. POTH, M.D., F.A.C.S., Galveston.
Atelectasis and Pneumonitis as a Postoperative Complication; Prevention and Treatment. HENRY K. BEECHER, M.D., Boston.

GASTROINTESTINAL TRACT

JOHN D. STEWART, M.D., F.A.C.S., Buffalo, *Chairman.*

Monday, 8:30—11:30 a.m., Eleventh Street Theatre

JOHN D. STEWART, M.D., F.A.C.S., Buffalo, *Moderator.*
Anomalies of the Gastrointestinal Tract and Their Surgical Significance. WILLIAM H. SNYDER, JR., M.D., F.A.C.S., Los Angeles.
Complications of Colostomy and Ileostomy. AMBROSE H. STORCK, M.D., F.A.C.S., New Orleans.
Management of Nonspecific Ulcerative Colitis. LELAND S. MCKITTRICK, M.D., F.A.C.S., Boston.
Question and Answer Period.
Trends in Gastric Surgery. WILLIAM P. LONGMIRE, JR., M.D., F.A.C.S., Los Angeles.
Polyps of the Colon. JAMES P. KIRTLEY, JR., M.D., F.A.C.S., Nashville.
Abdominal Incisions. PAUL A. KENNEDY, M.D., F.A.C.S., Buffalo.
Question and Answer Period.

Tuesday, 8:30—11:30 a.m., Eleventh Street Theatre

JOHN M. WAUGH, M.D., F.A.C.S., Rochester, Minn., *Moderator.*
Regional Enteritis. JOHN M. WAUGH, M.D., F.A.C.S., Rochester, Minn.
Pseudomembranous Enterocolitis. HARRY W. HALE, JR., M.D., F.A.C.S., Buffalo.
Some Aspects of Gastrointestinal Hormones. JOHN H. MULHOLLAND, M.D., F.A.C.S., New York.
Question and Answer Period.
Intestinal Obstruction: Panel Discussion.
JAMES D. RIVES, M.D., F.A.C.S., New Orleans, *Moderator.*
Participants: CLARENCE DENNIS, M.D., F.A.C.S., Brooklyn; ROBERT ELMAN, M.D., F.A.C.S., St. Louis; JAMES E. HIX, M.D., F.A.C.S., Owensboro, Kentucky.

Wednesday, 8:30—11:30 a.m., Eleventh Street Theatre

WALTER G. MADDOCK, M.D., F.A.C.S., Chicago, *Moderator.*
Management of the High Gastric Ulceration. WILLIAM F. RIENHOFF, JR., M.D., F.A.C.S., Baltimore.
Stomal Ulcer. WALTER G. MADDOCK, M.D., F.A.C.S., Chicago.
Management of Perforative Carcinoma of the Colon. GORDON A. DONALDSON, M.D., F.A.C.S., Boston.
Question and Answer Period.
Surgery of Diaphragmatic Hernia. HOWARD H. BRADSHAW, M.D., F.A.C.S., Winston-Salem.
Antibiotics in Gastrointestinal Surgery. DERYL HART, M.D., F.A.C.S., Durham.
Parenteral Feeding. DAVID V. HABIF, M.D., F.A.C.S., New York.
Problems in Radiological Diagnosis of Surgical Lesions of the Gastrointestinal Tract. DONALD W. S. STIFF, M.D., Buffalo.
Question and Answer Period.

Thursday, 8:30—11:30 a.m., Eleventh Street Theatre

R. KENNEDY GILCHRIST, M.D., F.A.C.S., Chicago, *Moderator.*
Carcinoma of the Anus. R. KENNEDY GILCHRIST, M.D., F.A.C.S., Chicago.
Massively Bleeding Peptic Ulcer. CALVIN M. SMYTH, JR., M.D., F.A.C.S., Philadelphia.
The Problem of Reconstruction After Esophageal Resection. RICHARD H. SWEET, M.D., F.A.C.S., Boston.
Question and Answer Period.
Peritonitis: Panel Discussion.
CHAMP LYONS, M.D., F.A.C.S., Birmingham, *Moderator.*
Participants: J. GARROTT ALLEN, M.D., F.A.C.S., Chicago; CLARENCE E. GARDNER, JR., M.D., F.A.C.S., Durham; RUDOLF J. NOER, M.D., F.A.C.S., Louisville.

DISEASES OF THE LIVER, BILIARY TRACT, AND PANCREAS

ROBERT M. ZOLLINGER, M.D., F.A.C.S., Columbus, *Chairman.*

Monday, 8:30—11:30 a.m., South Ballroom

SURGICAL ASPECTS OF THE LIVER

CARL A. MOYER, M.D., F.A.C.S., St. Louis, *Moderator.*
Liver Injuries. HOWARD E. SNYDER, M.D., F.A.C.S., Winfield, Kansas.
Lobectomy for Malignancy in Children. H. WILLIAM CLATWORTHY, JR., M.D., F.A.C.S., Columbus.
Surgical Aspects of Hepatic Malignancy in Adults. EUGENE M. BRICKER, M.D., F.A.C.S., St. Louis.
Management of Hepatic Coma. BEN EISEMAN, M.D., F.A.C.S., Denver.
Indications for Venous Shunt for Portal Hypertension. ROBERT R. LINTON, M.D., F.A.C.S., Brookline.
Surgical Therapy Other Than Shunts for Portal Hypertension. LOUIS M. ROUSSELOT, M.D., F.A.C.S., New York.
Present Status of Hepatic Artery Ligation. WILLIAM A. ALTEMEIER, M.D., F.A.C.S., Cincinnati.
Evaluation of the Surgical Patient—Importance of Liver Function Survey. CARL A. MOYER, M.D., F.A.C.S., St. Louis.

Monday, 10:30—11:30 a.m.

Panel Discussion.

CARL A. MOYER, M.D., F.A.C.S., St. Louis, *Moderator.*
Participants: HOWARD E. SNYDER, M.D., F.A.C.S., Winfield; H. WILLIAM CLATWORTHY, M.D., F.A.C.S., Columbus; EUGENE M. BRICKER, M.D., F.A.C.S., St. Louis; BEN EISEMAN, M.D., F.A.C.S., Denver; ROBERT R. LINTON, M.D., F.A.C.S., Brookline; LOUIS M. ROUSSELOT, M.D., F.A.C.S., New York; WILLIAM A. ALTEMEIER, M.D., F.A.C.S., Cincinnati.

Tuesday, 8:30—11:30 a.m., South Ballroom

SURGERY OF THE GALLBLADDER

FREDERICK A. COLLER, M.D., F.A.C.S., Ann Arbor, *Moderator.*

Evaluation of the Evidence for Cholecystectomy. ROBERT T. TIDRICK, M.D., F.A.C.S., Iowa City.

Preoperative Survey of the Patient with Gallbladder Disease. WILLIAM D. HOLDEN, M.D., F.A.C.S., Cleveland.

Early Surgery for Acute Cholecystitis. J. ENGLEBERT DUNPHY, M.D., F.A.C.S., Boston.

Delayed Surgery for Acute Cholecystitis. RUSSELL L. MUSTARD, M.D., F.A.C.S., Battle Creek.

Technical Considerations in Safe Cholecystectomy. FREDERICK A. COLLER, M.D., F.A.C.S., Ann Arbor.

The Management of Gallbladder Symptoms Following Previous Biliary Surgery. CALVIN M. SMYTH, JR., M.D., F.A.C.S., Abington.

Polyps and Carcinoma of the Gallbladder. ROBERT J. COFFEY, M.D., F.A.C.S., Washington, D. C.

The Significance of Cardiac Symptoms in Biliary Surgery. I. S. RAVDIN, M.D., F.A.C.S., Philadelphia.

Tuesday, 10:30—11:30 a.m.

Panel Discussion.

FREDERICK A. COLLER, M.D., F.A.C.S., Ann Arbor, *Moderator.*

Participants: ROBERT T. TIDRICK, M.D., F.A.C.S., Iowa City; WILLIAM D. HOLDEN, M.D., F.A.C.S., Cleveland; J. ENGLEBERT DUNPHY, M.D., F.A.C.S., Boston; RUSSELL L. MUSTARD, M.D., F.A.C.S., Battle Creek; CALVIN M. SMYTH, JR., M.D., F.A.C.S., Abington; ROBERT J. COFFEY, M.D., F.A.C.S., Washington; I. S. RAVDIN, M.D., F.A.C.S., Philadelphia.

Wednesday, 8:30—11:30 a.m., South Ballroom

SURGERY OF THE BILE DUCTS

ARTHUR W. ALLEN, M.D., F.A.C.S., Boston, *Moderator.*

Indications and Technique of Operative Cholangiography. STANLEY O. HOERR, M.D., F.A.C.S., Cleveland.

Evaluation of Intravenous Cholangiography. FRANK GLENN, M.D., F.A.C.S., New York.

Indications and Contraindications for Surgery in the Jaundiced Patient. WARREN H. COLE, M.D., F.A.C.S., Chicago.

Technique of Exploration of the Common Duct. ARTHUR W. ALLEN, M.D., F.A.C.S., Boston.

Surgical Technique in the Repair of Extrahepatic Bile Ducts. WALTMAN WALTERS, M.D., F.A.C.S., Rochester, Minn.

Choice of Surgical Procedures for Relief of Obstructive Jaundice Due to Malignancy. ALTON OCHSNER, M.D., F.A.C.S., New Orleans.

Wednesday, 10:30—11:30 a.m.

Panel Discussion.

ARTHUR W. ALLEN, M.D., F.A.C.S., Boston, *Moderator.*

Participants: FRANK GLENN, M.D., F.A.C.S., New York; STANLEY O. HOERR, M.D., F.A.C.S., Cleveland; WARREN H. COLE, M.D., F.A.C.S., Chicago; WALTMAN WALTERS, M.D., F.A.C.S., Rochester, Minn.; ALTON OCHSNER, M.D., F.A.C.S., New Orleans.

Thursday, 8:30—11:30 a.m., South Ballroom

SURGICAL DISEASES OF THE PANCREAS

JOHN H. MULHOLLAND, M.D., F.A.C.S., New York, *Moderator.*

Role of Trypsin in the Pathogenesis of Acute Pancreatitis. SAMUEL R. POWERS, JR., M.D., Albany.

The Use of Blood and Albumin in the Treatment of Pancreatitis. HENRY N. KENWELL, M.D., F.A.C.S., Buffalo.

Diagnosis and Treatment of Postoperative Pancreatitis. E. THOMAS BOLES, M.D., Columbus.

Management of Cysts of the Pancreas. VINTON E. SILER, M.D., F.A.C.S., Cincinnati.

Evaluation of Sphincterotomy. JOHN H. MULHOLLAND, M.D., F.A.C.S., New York.

Surgical Treatment of Chronic Recurrent Pancreatitis. JAMES T. PRIESTLEY, M.D., F.A.C.S., Rochester, Minn.

Diagnosis and Treatment of Adenomas of the Pancreas. EDWIN H. ELLISON, M.D., F.A.C.S., Columbus.

Indications and Contraindications to Resection of Carcinoma of the Head of the Pancreas. ROBERT ELMAN, M.D., F.A.C.S., St. Louis.

Thursday, 10:30—11:30 a.m.

Panel Discussion.

JOHN H. MULHOLLAND, M.D., F.A.C.S., New York, *Moderator.*

Participants: SAMUEL R. POWERS, JR., M.D., Albany; HENRY N. KENWELL, M.D., F.A.C.S., Buffalo; E. THOMAS BOLES, M.D., Columbus; VINTON E. SILER, M.D., F.A.C.S., Cincinnati; JAMES T. PRIESTLEY, M.D., F.A.C.S., Rochester, Minn.; EDWIN H. ELLISON, M.D., F.A.C.S., Columbus; ROBERT ELMAN, M.D., F.A.C.S., St. Louis.

OBSTETRIC AND GYNECOLOGIC SURGICAL CARE

JOHN I. BREWER, M.D., F.A.C.S., Chicago, *Chairman.*

Monday, 8:30—11:30 a.m., Gold Room, Congress Hotel

Forceps and Versions. WILLIAM F. MENGERT, M.D., Chicago.
Cesarean Section. SAMUEL A. COSGROVE, M.D., F.A.C.S., Jersey City.
The Legal Aspects of Artificial Insemination. ALLEN D. HOLLOWAY, Chicago.

Tuesday, 8:30—11:30 a.m.

The Function of Hospital Departments and Tissue Committees. LEON P. FOX, M.D., F.A.C.S., San Jose, California.
Justifiable Hysterectomies. GEORGE H. GARDNER, M.D., F.A.C.S., Chicago.
Sterilization. M. EDWARD DAVIS, M.D., F.A.C.S., Chicago.
The Manchester Operation. STUART ABEL, M.D., F.A.C.S., Chicago.

Wednesday, 8:30—11:30 a.m.

Carcinoma of the Cervix and the Childbearing Function. HERBERT E. SCHMITZ, M.D., F.A.C.S., Chicago.
Carcinoma of the Breast and the Childbearing Function. FRANK E. ADAIR, M.D., F.A.C.S., New York.
Carcinoma of the Thyroid and Hyperthyroidism and the Childbearing Function. DWIGHT E. CLARK, M.D., F.A.C.S., Chicago.

Thursday, 8:30—11:30 a.m.

Analgesic and Anesthetic Drugs and Their Action. MAX S. SADOVE, M.D., Chicago.
The Use of Analgesics and Anesthetics in Obstetrics. RALPH A. REIS, M.D., F.A.C.S., Chicago.
Practical Clinical Aspects of Erythroblastosis. EDITH L. POTTER, M.D., Chicago.
Hypofibrinogenemia. C. PAUL HODGKINSON, M.D., F.A.C.S., Detroit.

Friday, 8:30—11:30 a.m.

Vaginal Hysterectomy. EDWARD D. ALLEN, M.D., F.A.C.S., Chicago.
Pelvic Lesions Complicating Pregnancy. JOHN PARKS, M.D., F.A.C.S., Washington, D. C.
Urinary Incontinence in the Female. C. PAUL HODGKINSON, M.D., F.A.C.S., Detroit; VINCENT J. O'CONOR, M.D., F.A.C.S., Chicago.

NEOPLASMS OF THE MUSCULOSKELETAL SYSTEM; DIAGNOSIS, TREATMENT, AND PROGNOSIS

MURRAY M. COPELAND, M.D., F.A.C.S., Washington, D. C., *Chairman.*

Monday, 8:30—11:30 a.m., Lincoln Room, Congress

Cartilaginous Tumors of Bone—Diagnosis, Treatment, and Prognosis.
Primary Osteoblastic Neoplasms of Bone—Diagnosis, Treatment, and Prognosis.

Intermission

Remarks on Malignant Bone Tumors.
Evaluation of Radioisotopes as an Adjunct to Diagnosis and Treatment of Bone Lesions.
Discussion.

Tuesday, 8:30—11:30 a.m.

Periosteal Osteomas, Differential Diagnosis, Treatment, and Prognosis.
Giant Cell Tumors, and Bone Cysts, Differential Diagnosis, Treatment, and Prognosis.

Intermission

Diagnosis and Treatment of Metastatic Lesions in Bone.
Discussion.

Wednesday, 8:30—11:30 a.m.

Clinical Consideration of Malignant Bone Tumors in Children.
Massive Resection in the Treatment of Bone Sarcoma.

Intermission

Radical Amputations in the Treatment of Malignant Bone Tumors (Forequarter, and Hemipelvectomy).
Discussion.

Thursday, 8:30—11:30 a.m.

Fibrosarcoma of Bone and Soft Parts, Rhabdomyosarcoma, and Others; Diagnosis, Treatment, and Prognosis.
Granulomatous Tumors Involving Bone Which Simulate Primary Bone Tumors.

Intermission

Ewing's Tumor, Reticulum Sarcoma, and Multiple Myeloma; Diagnosis, Treatment, and Prognosis.
Discussion.

Speakers and participants in the program will include:
MURRAY M. COPELAND, M.D., F.A.C.S., Washington, D. C.
CHARLES F. GESCHICKTER, M.D., Washington, D. C.
C. HOWARD HATCHER, M.D., Chicago.
NORMAN L. HIGINBOTHAM, M.D., F.A.C.S., New York.
HENRY R. MCCARROLL, M.D., St. Louis.
SIR HARRY PLATT, M.D., F.A.C.S., F.R.C.S., Manchester, England.
MARY S. SHERMAN, M.D., F.A.C.S., New Orleans.
HUGH SMITH, M.D., F.A.C.S., Memphis.
H. HERMAN YOUNG, M.D., F.A.C.S., Rochester, Minn.

SURGERY OF THE HAND

MICHAEL L. MASON, M.D., F.A.C.S., Chicago, *Chairman.*

Monday—Thursday, 8:30—11:30 a.m., Florentine Room, Congress Hotel

Scope and Development of Surgery of the Hand. SUMNER L. KOCH, M.D., F.A.C.S., Chicago.
Anatomy of the Hand. BARRY J. ANSON, PH.D.(MED. SC.), Chicago.
Management of Sharp Lacerated Wounds of the Hand. JOSEPH L. POSCH, M.D., F.A.C.S., Detroit.
Management of Crushing Injuries of the Hand. JOHN L. BELL, M.D., F.A.C.S., Chicago.
Management of Fractures of the Bones of the Hand. J. EDWARD FLYNN, M.D., F.A.C.S., Boston.
Care of Infected Injuries and Injuries Seen Late. WILLIAM H. FRACKELTON, M.D., F.A.C.S., Milwaukee.
Secondary Nerve and Tendon Repair. JOSEPH H. BOYES, M.D., Los Angeles.
Burns of the Hand. BRADFORD CANNON, M.D., F.A.C.S., Boston.
Skin Replacement in Surgery of the Hand. DARREL T. SHAW, M.D., F.A.C.S., Cleveland.
Tendon Transfers in Reparative and Reconstructive Surgery of the Hand. DANIEL C. RIORDAN, M.D., New Orleans.
Congenital Anomalies of the Hand. ARTHUR J. BARSKY, M.D., New York.
Dupuytren's Contracture and Tumors of the Hand. MICHAEL L. MASON, M.D., F.A.C.S., Chicago.

CARDIOVASCULAR SURGERY

C. WALTON LILLEHEI, M.D., F.A.C.S., Minneapolis, *Chairman.*

Monday—Thursday, 8:30—11:30 a.m., Upper Tower

Participants and topics will appear in the official Congress Program and the November issue of the *Bulletin.*

SURGICAL ASPECTS OF PULMONARY DISEASE

HERBERT C. MAIER, M.D., F.A.C.S., New York, *Chairman.*

Monday, 8:30—11:30 a.m., Francis I, Congress Hotel

PULMONARY SURGERY OF INFANCY AND CHILDHOOD
Endoscopic Aspects of Airway Obstruction in Infancy and Childhood. PAUL H. HOLINGER, M.D., F.A.C.S., Chicago.
Acquired and Congenital Lung Cysts: Their Differentiation and Treatment. WILLIS J. POTTS, M.D., F.A.C.S., Chicago.
Vascular Anomalies of the Lungs. HERBERT C. MAIER, M.D., F.A.C.S., New York.
Surgical Treatment of Pulmonary Infections. MARK M. RAVITCH, M.D., F.A.C.S., New York.

Panel Discussion: Pulmonary Surgery of Infancy and Childhood.
WILLIS J. POTTS, M.D., F.A.C.S., Chicago, *Moderator.*
PAUL H. HOLINGER, M.D., F.A.C.S., Chicago.
HERBERT C. MAIER, M.D., F.A.C.S., New York.
MARK M. RAVITCH, M.D., F.A.C.S., New York.

Tuesday, 8:30—11:30 a.m.

PHYSIOLOGIC FACTORS IN OPERATIVE AND POSTOPERATIVE MANAGEMENT
Anoxia in Pulmonary Surgery. WILLIAM E. ADAMS, M.D., F.A.C.S., Chicago.
Respiratory Acidosis. WILL C. SEALY, M.D., Durham.
Significance of Pulmonary Hypertension. WILLIAM E. ADAMS, M.D., F.A.C.S., Chicago.
Panel Discussion: Clinical Application of Physiologic Principles in Lung Surgery.
HERBERT C. MAIER, M.D., F.A.C.S., New York, *Moderator.*
WILLIAM E. ADAMS, M.D., F.A.C.S., Chicago.
WILL C. SEALY, M.D., Durham.

Wednesday, 8:30—11:30 a.m.

PULMONARY NEOPLASMS
Bronchial Adenomas. LAMAR SOUTTER, M.D., F.A.C.S., Boston.
Bronchogenic Carcinoma:
Technique and Results of Radical Pneumonectomy. JOHN L. POOL, M.D., F.A.C.S., New York.
Experiences with Surgery Combined with Radiotherapy. DAVID P. BOYD, M.D., F.A.C.S., Boston.
Results of Pulmonary Resection in Relation to Cell Type. O. THERON CLAGETT, M.D., F.A.C.S., Rochester, Minn.
Panel Discussion: Pulmonary Neoplasms (Including Pleural and Tracheal Tumors).
O. THERON CLAGETT, M.D., F.A.C.S., Rochester, Minn., *Moderator.*
DAVID P. BOYD, M.D., F.A.C.S., Boston.
JOHN L. POOL, M.D., F.A.C.S., New York.
LAMAR SOUTTER, M.D., F.A.C.S., Boston.

Thursday, 8:30—11:30 a.m.

(Program in part)
Panel Discussion: Current Surgical Treatment of Pulmonary Tuberculosis.
PAUL C. SAMSON, M.D., F.A.C.S., Oakland, *Moderator.*

Symposium on Trauma

Tuesday, 2:00—5:00 p.m., Blackstone Theatre

R. ARNOLD GRISWOLD, M.D., F.A.C.S., Louisville, Chairman, Committee on Trauma, American College of Surgeons, *Presiding.*
Automobile Accidents. MR. JOHN O. MOORE, Cornell University, New York; C. HUNTER SHELDEN, M.D., F.A.C.S., Pasadena; ROSS A. MCFARLAND, PH.D., Boston.
Traumatic Injuries to the Liver. JOHN HOWARD, M.D., Houston; MICHAEL E. DEBAKEY, M.D., F.A.C.S., Houston.
Highway Accidents. GEORGE J. CURRY, M.D., F.A.C.S., Flint, Mich.
Transportation of the Injured Within the Hospital. DAVID R. LIMBACH, M.D., Flint, Mich.

Symposium on Cancer

Wednesday, 2:00—5:00 p.m., Blackstone Theatre

DANELY P. SLAUGHTER, M.D., F.A.C.S., Chicago, Chairman, Committee on Cancer, American College of Surgeons, *Presiding.*
The Choice of Treatment in Breast Cancer. SIR STANFORD CADE, F.R.C.S., London.
Papillary Thyroid Carcinoma. EDGAR L. FRAZELL, M.D., F.A.C.S., New York.
Surgical Implications of Radiotherapy. HOWARD HUNT, M.D., Omaha.
Tumor Cell Contamination in Cancer Surgery. LAUREN V. ACKERMAN, M.D., St. Louis.
Malignant Tumors of the Endometrium. HERBERT E. SCHMITZ, M.D., F.A.C.S., Chicago.

Symposium on Graduate Training in Surgery and the Surgical Specialties

Thursday, 1:30—3:00 p.m., Blackstone Theatre

FREDERICK A. COLLER, M.D., F.A.C.S., Ann Arbor, *Chairman.*

Title to be announced. JOSEPH R. SHAEFFER, (M.C.) Colonel, U.S.A., F.A.C.S., Washington, D. C.

Essentials of Approved Residency in General Surgery. WARFIELD M. FIROR, M.D., F.A.C.S., Baltimore.

Essentials of Approved Residency in Otolaryngology. JAMES H. MAXWELL, M.D., F.A.C.S., Ann Arbor.

Tripartite Residency Review Committees in Surgical Specialties. GEORGE W. STEPHENSON, M.D., F.A.C.S., Chicago.

Education of Foreign Residents. FREDERICK A. COLLER, M.D., F.A.C.S., Ann Arbor.

Motion Picture Symposium: New or Unusual Problems in Surgery

Wednesday, 7:30—10:00 p.m., Grand Ballroom

B. MARDEN BLACK, M.D., F.A.C.S., Rochester, Minn., *Presiding.*

Chylous Cyst of Mesentery. ROWENA SPENCER, M.D., New Orleans.

Annular Pancreas with Obstruction of Duodenum. RUDOLF J. NOER, M.D., F.A.C.S., and HUGH B. LYNN, M.D., Louisville.

Parathyroid Adenoma in Pericardium. O. THERON CLAGETT, M.D., F.A.C.S., Rochester, Minn.

Iliac Vena Caval Fistula. HARRIS B. SHUMACKER, JR., M.D., F.A.C.S., Indianapolis.

Automobile Fractures of the Larynx. PAUL H. HOLINGER, M.D., F.A.C.S., and PAUL W. GREELEY, M.D., F.A.C.S., Chicago.

Ulcer Diathesis Associated with Islet Cell Tumor of the Pancreas. ROBERT M. ZOLLINGER, M.D., F.A.C.S., and EDWIN H. ELLISON, M.D., F.A.C.S., Columbus.

Double Superior Vena Cava. ELLIOTT S. HURWITT, M.D., F.A.C.S., New York.

Presentation of 1954 Motion Picture Award for Outstanding Educational Value to Dr. Lawrence Chaffin. HILGER P. JENKINS, M.D., F.A.C.S., Chicago.

Gastrointestinal Polyps Associated with Oral Pigmentations Peutz-Jeghers Syndrome. JOHN M. WAUGH, M.D., F.A.C.S., Rochester, Minn.

Surgical Treatment of Congenitally Absent Aortic Arch. J. MAXWELL CHAMBERLAIN, M.D., F.A.C.S., New York.

Extrauterine Pregnancy Delivered at Term. MILTON L. MCCALL, M.D., F.A.C.S., New Orleans.

Surgical Treatment of Dissecting Aneurysm of the Aorta. MICHAEL E. DEBAKEY, M.D., F.A.C.S., Denton A. COOLEY, M.D., F.A.C.S., and OSCAR CREECH, M.D., F.A.C.S., Houston.

Television Program, University of Illinois Research and Educational Hospitals

Co-ordinators and panel personnel to be announced.

Monday, 9:00 a.m.—12:00 noon; 2:00—5:00 p.m., Williford Ballroom

Segmental Pulmonary Resection. WILLARD VAN HAZEL, M.D., F.A.C.S.

Pneumonectomy for Carcinoma. ROBERT J. JENSIK, M.D., F.A.C.S.

Parotidectomy for Tumor. HARRY W. SOUTHWICK, M.D., F.A.C.S.

Radical Mastectomy for Carcinoma. WILLIAM J. GROVE, M.D.

Tuesday, 9:00 a.m.—12:00 noon; 2:00—5:00 p.m.

Elevation of Depressed Skull Fracture. ERIC OLDBERG, M.D., F.A.C.S.

Radical Neck Dissection with Hemimandibulectomy for Carcinoma of the Gingiva. DANELY P. SLAUGHTER, M.D., F.A.C.S.

Thyroidectomy for Adenoma. WARREN H. COLE, M.D., F.A.C.S.

Gastrectomy for Duodenal Ulcer. WARREN H. COLE, M.D., F.A.C.S.

Wednesday, 9:00 a.m.—12:00 noon; 2:00—5:00 p.m.

Laminectomy for Disc. CLAUDE N. LAMBERT, M.D.
Peripheral Vascular Surgery. GEZA DE TAKATS, M.D., F.A.C.S.
Fracture Operations. CLAUDE N. LAMBERT, M.D.
Skin Grafts. PAUL W. GREELEY, M.D., F.A.C.S.

Thursday, 9:00 a.m.—12:00 noon; 2:00—5:00 p.m.

Cholecystectomy and Choledochostomy for Cholelithiasis. CHARLES B. PUESTOW, M.D., F.A.C.S.
Total Abdominal Hysterectomy. WILLIAM MENGERT, M.D.
Cardiovascular Surgery. ORMAN C. JULIAN, M.D., F.A.C.S.
Abdominal Perineal Resection of the Rectum for Carcinoma. JOHN T. REYNOLDS, M.D., F.A.C.S.

Friday, 9:00 a.m.—12:00 noon; 2:00—5:00 p.m.

Retropubic Prostatectomy for Prostatic Hypertrophy. JOSEPH H. KIEFER, M.D., F.A.C.S.
Vaginal Hysterectomy. WILLIAM MENGERT, M.D.
Hypothermia. MAX SADOVE, M.D.
Lobectomy for Bronchiectasis. EDWARD J. BEATTIE, JR., M.D., F.A.C.S.

Trauma Oration

Thursday, 3:15—3:45 p.m., Grand Ballroom

ALFRED BLALOCK, M.D., F.A.C.S., Baltimore; President, American College of Surgeons, *Presiding*.
Mass Casualties. FRANK B. BERRY, M.D., F.A.C.S., Washington, D. C.; Assistant Secretary of Defense, Health and Medicine.

Forum on Fundamental Surgical Problems

Monday, 9:00 a.m.–12:00 noon, Waldorf Ballroom and Normandy Lounge

HEART AND GREAT VESSELS

Dynamics of Blood Flow in Major Arteries and in Graft Disproportions. SIGMUND A. WESOLOWSKI, LESTER R. SAUVAGE, ROGER D. PING, and CHARLES C. FRIES, New York.
The Effect of Hypercholesterolemia on Canine Aortic Substitutes. OSCAR CREECH, JR., GEORGE L. JORDAN, JR., and MICHAEL E. DEBAKEY, Houston.
Experimental Closure of Ventricular Septal Defects. JUDAH FOLKMAN, Boston.
The Creation and Repair of Interventricular Septal Defects Under Direct Vision with a Heart-Lung Machine. JACKSON H. STUCKEY, BERNARD S. LEVOWITZ, CLARENCE DENNIS, EUGENE J. GORAYEB, HARRY ITICOVICI, LAVONNE A. YOUNG, MELVIN M. NEWMAN, and MARIE KERNAN, New York.
The Importance of Coronary Blood Flow to the Incidence of Ventricular Fibrillation in the Cold Canine Heart—I, Pharmacological Evidence on the Role of Hypoxia. SYLVAN B. BAER, A. VERNON MONTGOMERY, EMIL BLAIR, and HENRY SWAN, Denver.
Method for the Prevention of Ventricular Fibrillation During Hypothermia. CHARLES A. HUFNAGEL, Washington, D. C.
Myocardial failure in Experimental Hypothermia. LEO R. RADIGAN, THOMAS A. LOMBARDO, and ANDREW G. MORROW, Bethesda.
Evaluation of the Mechanical Shunt to By-Pass the Thoracic Aorta Including the Arch. FREDERICK S. CROSS, STEPHEN S. HUDACK, EARLE B. KAY, and YOICHI HIROSE, Cleveland.
The Use of Carbon Dioxide to Prevent Ventricular Fibrillation in Intracardiac Surgery During Hypothermia. F. JOHN LEWIS and SUAD A. NIAZI, Minneapolis.
Accurate Diagnostic Coronary Arteriaography in the Dog. JACK A. CANNON, CHARLES A. CLIFFORD, GAUTAM DIESH, and WILEY F. BARKER, Los Angeles.
Avoidance of Renal Ischemia During Resection of the Abdominal Aorta Including the Renal Arteries. ELLIOTT S. HURWITT, STANLEY F. ALTMAN, BERNARD SEIDENBERG, and HENRY HAIMOVICI, New York.

INFECTIONS AND BURNS

The Serum Properdin Titers in Surgical Patients. JERREL W. BENSON, WILLIAM E. ABBOTT, WILLIAM D. HOLDEN, and STANLEY LEVEY, Cleveland.
Bacterial Invasion in Experimental Burns. PHILIP B. PRICE, C. REED BROWN, ROBERTA C. PEEK, and LARUE HINCKLEY, Salt Lake City.

The Enzymes Found in Granulations. EDWARD L. HOWES, New York.
The Concentration of Risa by Abscesses—A Diagnostic Tool. IRVING M. ARIEL, JEAN KUZNIK, and GEORGE T. PACK, JR., New York.
Thermal Burns in Man—X, Physiologic Studies. JAMES D. HARDY, Jackson, Miss.
Effects of Local Chilling in the Treatment of Burns. LEVI E. REYNOLDS, C. REED BROWN, and PHILIP B. PRICE, Salt Lake City.
Local Edema and Capillary Permeability associated with Burn Wounds. THOMAS C. KING, PHILIP B. PRICE, LEVI REYNOLDS, and C. REED BROWN, Salt Lake City.
The Effect of Thermal Injury on Insensible Weight Loss in the Rat. H. C. MORGAN, R. P. ANDREWS, and M. J. JURKIEWICZ, St. Louis.
The Relationship of Dietary Protein to the Healing of Experimental Burns. R. P. ANDREWS, H. C. MORGAN, and M. J. JURKIEWICZ, St. Louis.
The Influence of Growth Hormone on the Nitrogen Balance of the Severely Burned. JOHN F. PRUDDEN, ELINOIR PEARSON, and HARRY S. SOROFF, Fort Sam Houston.

Monday, 2:00–5:00 p.m.

GASTROINTESTINAL TRACT

The Value of Vagotomy and Finney Pyloroplasty in Preventing Esophagitis After Cardioesophagectomies in Dogs. GEORGE W. GIRVIN and K. ALVIN MERENDINO, Seattle.
The Importance of Esophagoduodenal Continuity Following Total Gastrectomy. FREDERICK M. BINCKLEY, RICHARD E. GARDNER, and H. J. MCCORKLE, San Francisco.
Supplemental Experiments in Synthetic Esophageal Reconstruction. EDGAR F. BERMAN, Baltimore.
Gastric Secretion Studies Following Pituitary—Stalk Section in Dogs. THOMAS A. JOHNSON, JR., ALAN B. ROTHBALLER, S. C. SKORYNA, and DONALD R. WEBSTER, Quebec.
Studies in Curling's Ulcers. ROBERT P. HUMMEL, BERNARD BALIKOV, ROBERT D. PILLSBURY, and CURTIS P. ARTZ, Fort Sam Houston.
Mechanism of Ulcer Recurrence After the Antrum Exclusion Operation. EDWARD R. WOODWARD and VICTOR C. TILLMANNS, Los Angeles.
Effect of Hemigastrectomy, Gastroduodenostomy, and Vagotomy on Growth in Puppies. JACK A. THOMPSON, JOSEPH A. BONTA, and H. WILLIAM CLATWORTHY, Columbus.
The Effect of Resection of the Duodenum on Gastric Secretion of Hydrochloria Acid. EDWIN L. BRACKNEY and ALAN P. THAL, Minneapolis.
Alterations in Cardiac Output and Stroke Volume During the Dumping Syndrome. LEO D. KLAUBER, J. W. POPPELL, H. T. RANDALL, and K. E. ROBERTS, New York.
Aseptic Decompression of Experimentally Produced Intestinal Distention. ROBERT C. LIEN and WALTER G. MADDOCK, Chicago.
Strangulation Obstruction—Thirty Fistula Studies. ISIDORE COHN, JR., New Orleans.
Comparative Studies of the Water Absorbing Capacity of the Distal Small Intestine and the Colon. JOHN F. PERRY, JR., Minneapolis.

PLASTIC SURGERY

Common Antigenicity Between Skin Grafts and Total Lung Transplants. CREIGHTON A. HARDIN, Kansas City.
Homologous Skin Grafts as Altered by Passage in Vitro. HERBERT CONWAY, RICHARD B. STARK, and JEAN SEDAR, New York.
The Uptake of Radioactive Isotopes by in Vivo Tissue Culture Transplants in Diffusion Chambers. CLIFFORD L. KIEHN, Cleveland.
Mechanisms of Homograft Rejection. M. T. EDGERTON, J. D. DESPREZ, P. J. EDGERTON, and H. PETERSON, Baltimore.
Recall Phenomena in Human Skin Homografts. JOHN MARQUIS CONVERSE and FELIX T. RAPAPORT, New York.
Enzymatic Activity in Preserved Skin. JAMES T. CHAMNESS and FALLIS B. HERSHEY, St. Louis.
Postmortem Homografts, Laboratory Investigations of Skin Viability Following Preservation by Various Methods. JAMES BARRETT BROWN, MINOT P. FRYER, and THOMAS J. ZAYDON, St. Louis.
Report on the Effectiveness of Sterilization of Canine Costal Cartilage by Cobalt 60 Irradiation and Its Fate When Used as Homografts. JOHN D. LYNCH, RICHARD B. ASBURY, and REED O. DINGMAN, Ann Arbor.
*p*H Ion Concentration and Skin Grafting. RICHARD C. YE and SHERMAN F. SAFFIER, Kansas City.

UROLOGY

An Experimental Comparison of Renal Damage and Electrolyte Imbalance Following Various Methods of Urinary Deviation. W. T. IRVINE, C. MCC. ALLAN, and D. R. WEBSTER, Montreal.

Evaluation of Plasma Electrolytes and Renal Function in Patients with Sigmoid Urinary Pouches. FRANK A. PERRY, MICHAEL R. DEDDISH, and KATHLEEN E. ROBERTS, New York.

Absorption of Urinary Constituents from Various Segments of the Gastrointestinal Tract Used as Urinary Conduits or Reservoirs. JOHN J. MURPHY and CLETUS W. SCHWEGMAN, Philadelphia.

Metabolic Alterations in Surgical Patients—VII, the Relief of Lower Urinary Tract Obstruction. LESTER PERSKY, JERREL W. BENSON, STANLEY LEVEY, and WILLIAM B. ABBOTT, Cleveland.

Function of Striated Muscle in Control of Urination—I, Effect of Pudendal Block. JACK LAPIDES, HOWARD O. GRAY, and JOHN C. FAWLING, Ann Arbor.

Function of Striated Muscle in Control of Urination—II, Effect of Complete Skeletal Muscle Paralysis. JACK LAPIDES, ROBERT B. SWEET, and LOUIS W. LEWIS, Ann Arbor.

Surgical Reconstruction of the Ureter by a New Technique. WILLIAM C. SHOEMAKER and ROBERT BOWER, Philadelphia.

Total Bladder Substitution Using Seromuscular Grafts. WILLIAM C. SHOEMAKER and PAUL J. GROTZINGER, Philadelphia.

Determination of the Period of Occlusion of the Renal Arteries in the Experimental Animal Compatible with Survival. WILLIAM J. MCCANN and JOHN L. MADDEN, New York.

The Protective Effect of Subfiltration Arterial Pressure on the Kidney. GEORGE C. MORRIS, CHARLES HEIDER, and JOHN H. MOYER, Houston.

Mechanisms Controlling Solubility of Stone-Forming Crystalloids. G. MILLER and C. W. VERMEULEN, Chicago.

The Renal Lymphatics. WILLARD E. GOODWIN and JOSEPH J. KAUFMAN, Los Angeles.

Renal Function Studies After Unilateral Nephrectomy and Denervation of the Remaining Kidney. ROGER BAKER and DUNCAN GOVAN, Washington, D. C.

The Effect of Ureteral Anastomosis Upon the Conduction of Peristalsis—an Electroureterographic Study. HARVEY R. BUTCHER, JR. and WILLIAM SLEATOR, JR., St. Louis.

Point Source Irradiation of Carcinoma of the Bladder (the Walter Reed Technique) MILTON FRIEDMAN, New York.

Tuesday, 9:00 a.m.–12:00 noon

HEART AND GREAT VESSELS

Myocardial Revascularization in the Dog: Effect of Creation of a Temporary Arterial-Left Auricular Fistula. LEWIS S. CAREY, MAURICE C. FUQUAY, JOHN H. GRINDLAY, and JOHN W. KIRKLIN, Rochester, Minn.

Myocardial Revascularization: a Comparison Between Internal-Mammary-Artery and Subclavian Artery Implantation in the Dog. MAURICE C. FUQUAY, LEWIS S. CAREY, JOHN W. KIRKLIN, and JOHN H. GRINDLAY, Rochester, Minn.

Coronary and Carotid Artery Perfusion During Total By-Pass of the Heart. ROBERT A. GAERTNER, JEROME HAROLD KAY, JAMES ISAACS, and RICHARD DEVER, Baltimore.

Brain Perfusion as an Aid to Open Cardiac Surgery. WILLIAM H. PENISTON and VICTOR RICHARDS, Los Angeles.

Circulatory By-Pass of the Right Heart—II, Further Observations on Vena Caval-Pulmonary Artery Shunts. JOSÉ PATIÑO, WILLIAM W. L. GLENN, PAUL H. GUILFOIL, MICHAEL HUME, and JOHN E. FENN, New Haven.

A Technique for Total By-Pass of the Heart. J. MAXWELL CHAMBERLAIN, New York.

Reservoir Circulation Without Mechanical Pumps for Intracardiac Surgery Under Direct Vision. J. C. CALLAGHAN and FRANK GERBODE, San Francisco.

Experimental Chronic Coronary Insufficiency Produced by Coronary Artery Embolization. GORDON MUNRO, J. CUTHBERT OWENS, and HENRY SWAN, Denver.

The Effects for the Hufnagel Valve on Renal Hemodynamics in Subjects with Aortic Valvular Insufficiency. GEORGE C. MORRIS, DENTON A. COOLEY, and JOHN H. MOYER, Houston.

A Prosthesis for the Correction of Mitral Insufficiency. RICHARD A. DEWALL, RICHARD L. VARCO, and C. W. LILLEHEI, Minneapolis.

METABOLISM AND NUTRITION

Evaluation of Body Composition in Surgical Disease Processes Utilizing a Method for the Simultaneous Determination of Red Cell Volume, Plasma Volume, Blood Volume, Total Body Water, Extracellular Water and Total Exchangeable Chloride, Sodium, and Potassium. J. D. MCMURREY, J. M. DAVIS, E. A. BOLING, and FRANCIS D. MOORE, Boston.

The Metabolic Responses to Anesthesia Without Trauma. LEROY D. VANDAM, THOMAS K. BURNAP, R. LENNIHAN, J. M. DAVIS, and FRANCIS D. MOORE, Boston.

Further Studies in Body Fluid Physiology—I, the Effect of 3 Per Cent Sodium Chloride, M/6 Sodium Lactate, and M/6 Ammonium Chloride on Plasma Carbon Dioxide Combining Power, pCO_2, and Blood *p*H. EDDIE E. BRAMLITT and JAMES D. HARDY, Memphis.

The Kinetics of Expander Transfer and Distribution from the Plasma Disappearance Curves. W. METCALF and L. M. ROUSSELOT, New York.

Studies on Intravenous Fat Emulsions. W. W. SHINGLETON, W. G. ANLYAN, M. H. WELLS, and M. SALEM, Durham, N. C.

The Development of a Preparation of Purified Animal Fat Suitable for Intravenous Use. MARY ANN PAYNE, NATHAN BROT, CLAUDE CHOLETTE, and JOHN M. BEAL, New York.

Relationship of Blood Protein Levels to Protein Reserve in the Body. DANIEL A. ALLENDE, Chicago.

Comparative Growth Studies of Puppies Receiving the Same Quantities of Protein as Oral Liver and Horse Meat with those Receiving Intravenous Plasma. EDWARD A. STEMMER, LOUIS R. HEAD, and J. GARROTT ALLEN, Chicago.

The Role of Bone Sodium in Electrolyte Balance and Surgery. JAMES H. CASEY and BERNARD ZIMMERMANN, Minneapolis.

Excretion of Aldosterone by the Postoperative Patient. BERNARD ZIMMERMANN, JAMES H. CASEY, HENRY S. BLOCH, EARL Y. BICKEL, and KALMAN GOVRIK, Minneapolis.

Tuesday, 2:00–5:00 p.m.

LIVER, BILIARY TRACT, and PANCREAS

Fat and Nitrogen Metabolism in Patients with Massive Small Bowel Resections. MORTON K. SCHWARTZ, ALBERT MEDWID, KATHLEEN E. ROBERTS, OSCAR BODANSKY, and HENRY T. RANDALL, New York.

Physiology of the Duodenum in Relation to the Biliary-Pancreatic System. Cinefluorophotographic Observations. HENRY DOUBILET, MAXWELL H. POPPEL, and JOHN H. MULHOLLAND, New York.

Selective Localization of Alkaloids in the Pancreas. GEORGE L. NARDI and JOHN SEIPEL, Boston.

Pancreatic and Biliary Intraductal Pressures. RENE B. MENGUY, GEORGE A. HALLENBECK, JESSE L. BOLLMAN, and JOHN H. GRINDLAY, Rochester, Minn.

The Comparative Effect of Plavolex and Blood in Experimental Sterile Lethal Hemorrhagic Pancreatitis. M. HARA, B. W. THOMPSON, and L. H. HUDSON, Little Rock.

The Absorption of Ascitic Fluid Following the Eversion of Intestinal Mucosa Within the Peritoneal Cavity. CHARLES G. NEUMANN, NINA S. BRAUNWALD, and J. WILLIAM HINTON, New York.

Removal of Blood Ammonia by Hemodialysis. JOHN E. KILEY, HAROLD F. WELCH, JOSEPH C. PENDER, and C. STUART WELCH, Albany.

The Role of Ammonia in the Production of Hepatic Coma. W. G. FOWLER, J. P. WHITE, G. CLARK, and B. EISEMAN, Denver.

The Effect of Glutamate Administration on Blood Ammonia Level and Its Correlation with Clinical Status in Patients with Hepatic Coma. DONALD M. PEARLMAN, New Haven.

Fluorescent Visualization of the Extrahepatic Biliary System Following Parenteral Hematoporphyrin Administration. D. S. RASMUSSEN-TAXDAL, RICHARD E. AHLQUIST, JR., and CHESTER E. HERROD, San Francisco, and GEORGE E. PECK, H. PATTERSON MACK, WILLIAM A. HOLBROOK, and FRANK H. J. FIGGE, Baltimore.

Wednesday, 9:00 a.m.–12:00 noon

CARDIOPULMONARY SUBJECTS

The Determination of Blood Flow Through Intact Human Arteries. ALBERTO FLORES, RICHARD T. MYERS, MERRILL SPENCER, and A. G. DENISON, Winston-Salem.

The Experimental Production of Intermittent Claudication. J. H. JACOBSON and F. F. MCALLISTER, New York.

An Experimental Study of Toxic Factors in Angiocardiography. J. GERARD MUDD, JULIO C. WONG, JOHN P. WYATT, and C. ROLLINS HANLON, St. Louis.

The Replacement of Long and Narrow Arterial Segments; a Comparative Experimental Study of Homografts, Heterografts, and Woven Plastic Prostheses. D. EMERICK SZILAGYI, CLAIBOURNE P. SHONNARD, and JUAN LOPEZ y LOPEZ, Detroit.

Cause and Prevention of Hemorrhage Following Extracorporeal Circulation. JOHN J. OSBORN, FRANK GERBODE, RONALD MCKENZIE, ANTHONY SHAW, and HERBERT A. PERKINS, San Francisco.

Hypotension: a comparison of the Differences in the Human Cerebral Hemodynamic and Metabolic Response to Drug-Induced and Acute Hemorrhagic Hypotension. H. H. STONE, T. N. MACKRELL, C. DONNELLY, M. TRUTER, and P. NEMIR, JR., Philadelphia.

A Vascular Anastomosis Clamp Allowing Rapid Reconstruction of Blood Flow. WILLIAM D. KELLY and John F. ALDEN, Minneapolis.

Experimental Myocardial Infarction Producted by Local Beta Radiation. PETER V. MOULDER, ROBERT W. HARRSION, WILLIAM E. ADAMS, and PAUL V. HARPER, Chicago.

Addition of Dead Space to Produce Hyperventilation for Prophylaxis of Atelectasis. SEYMOUR I. SCHWARTZ and W. ANDREW DALE, Rochester, N. Y.

The Experimental Production of Pulmonary Vascular Disease. J. F. DAMMANN, JR., RODNEY T. SMITH, and WILLIAM H. MULLER, JR., Charlottesville.

The Principles of Hyperventilation on the Treatment of Crushing Injuries to the Chest. E. T. MÖRCH, E. E. AVERY, and D. W. BENSON, Chicago.

COAGULATION, HYPOTHERMIA, AND STRESS

Studies on Serum Proteolytic Activity in Patients with Spontaneous Fibrinolysis. SAMUEL R. POWERS, JR. and HAROLD H. BROWNE, Albany.

Experimental Observations on the Influence of Hypothermia and Autonomolytic Drugs in Hemorrhagic Shock. ROBERT C. OVERTON and MICHAEL E. DEBAKEY, Houston.

Studies on the Bleeding Tendency Following Dextran Infusion. PAUL G. WEIL and DONALD R. WEBSTER, Montreal.

Bleeding After Large Transfusion of Citrated Blood. WILLIAM B. KIESWETTER and JACKSON HARRIS, Pittsburgh.

Effects of Hypothermia on Blood Coagulation. CECIL M. COUVES, ROBERT C. OVERTON, and W. E. EATON, Houston.

The Effect of Prolonged Hypothermia on Oxygen Consumption of the Liver Slice. E. J. FEDER, MORTON LEVINE, CLEM RUSS, and BERNARD FISHER, Pittsburgh.

Potassium Effects in the Hypothermic Dog. GEORGE E. MAVOR, R. ALLAN HARDER, GEORGE L. EMERSON, EARLE B. MAHONEY, and R. K. MCEVOY, Rochester, N. Y.

The Effect of Lowered Body Temperature on the Cerebral Hemodynamics and Metabolism of Man. H. H. STONE, T. N. MACKRELL, C. DONNELLY, M. TRUTER, and S. S. FROBESE, Philadelphia.

A Single Injection Method of Measuring Human Renal Plasma Flow. JACK A. THOMPSON, DONALD G. VIDT, MORRIS J. MANDEL, LEO A. SAPIRSTEIN, and ROBERT N. WATMAN, Columbus.

Stress Studies in Adrenalectomized Patients. HARVEY KREIGER, JERREL W. BENSON, C. JACKSON RAYBURN, WILLIAM E. ABBOTT, and STANLEY LEVEY, Cleveland.

Relationship of Experimental Renal Damage to Tolerance of Surgical Stress. EMILE J. MEINE, JR., Chicago.

Studies on the Completeness of Surgical Adrenalectomy. CHARLES ECKERT, T. E. WEICHSELBAUM, and HARRY W. MARGRAF, St. Louis.

Wednesday, 2:00–5:00 p.m.

LUNG, ENDOCRINES, AND TUMORS

Experimental Silicosis: Changes in the Disease in the Monkey Produced by "Arterializing" the Lung. H. WILLIAM SCOTT, JR., C. ROLLINS HANLON, BYRON J. OLSON, GEORGE L. FITE, and C. F. T. MATTERN, Bethesda.

Autonomic Control of the Pulmonary Vascular Bed—II, Detection of Pulmonary Edema with Sodium 22. MICHAEL G. WEIDNER, JR., AUDLEY O. BURFORD, ROLLIN A. DANIEL, JR., and RUDOLPH A. LIGHT, Nashville.

Studies on Perfusion of Human Blood Through Isolated Dog Lung. GILBERT S. CAMPBELL, NORMAN W. CRISP, and E. B. BROWN, JR., Minneapolis.

Comparative Protein Repletion in Cancer and Noncancer Cachexia. J. C. PEDEN, JR., J. S. RILEY, L. BOND, and M. D. MAXWELL, St. Louis.

A Plane Interstitial Isotope Applicator for Irradiation of the Mediastinum. PAUL V. HARPER, WILLIAM E. ADAMS, EMANUEL E. SCHWARTZ, ROBERT W. HARRISON, and K. A. LATHROP, Chicago.

A Simple Method of Implanting Radon Seeds Into the Pituitary Gland in the Treatment of Advanced Breast cancer. CHARLES F. W. ILLINGWORTH, A. P. M. FOREST, and D. A. PEEBLES BROWN, Glasgow.

Urine Calcium Excretion Studies as a Means of Selection of Hormone Dependent Tumors. A. G. JESSIMAN, Boston.

The Effect of Hypothermia on Malignant Growth in Rats. SUAD A. NIAZI and F. JOHN LEWIS, Minneapolis.

Secondary Kidney Homotransplantation. RICHARD H. EGDAHL and DAVID M. HUME, Minneapolis.

Renal Homotransplantation in Identical Twins. JOSEPH E. MURRAY, JOHN P. MERRILL, and J. HARTWELL HARRISON, Boston.

The Experimental Transplantation of Regenerated and Fetal Thyroid Tissue to the Spleen. H. J. MCCORKLE, ROBERT H. DERIEMER, DONALD HINE, ALBERT K. MINETA, and RUDOLPH O. F. OPPENHEIMER, San Francisco.

Arrest of Metatastic Mammary Carcinoma by Cortisone and Thyroid Therapy. H. M. LEMON, Boston.

Serum Kinetics of Thyroid Hormones in the Dog. T. M. MOORE and L. W. O'NEAL, St. Louis.

ORTHOPEDIC SURGERY

Further Experiments with Muscle Pedicle Bone Grafts. JOEL HARTLEY, New York.

Repair of Bone Transplant Fractures. MICHAEL BONFIGLIO, Iowa City.

P^{32} Exchange in Delayed Union of Fractures. FLOYD E. BLIVEN, JR., Rochester, N. Y.

Bone Metabolism: the Effect of a Sublethal Dose of Strontium 90 on Skeletal Metabolism. ROBERT D. RAY, N. KATHRYN WOLFF, DUNCAN THOMSON, and DUANE LAVIOLETTE, St. Louis.

Studies of Bone Growth Following Experimental Fractures of the Femur in Puppies. NICHOLAS R. GREVILLE and JOSEPH M. JANES, Rochester, Minn.

The Effect of Intramedullary Pins in Growing Bones. FREDERICK LEE LIEBOLT, N. Y.

Utilization of Radioactive Cobalt in the Sterilization of Homogenous Bone Transplants. PAUL H. DEVRIES, LLOYD KEMPE, and WADE O. BRINKER, Ann Arbor.

The Clinical Use of Cathode Ray Sterilized Grafts of Cadaver Bone, a Preliminary Report. C. ANDREW L. BASSETT, THOMAS F. HUDGINS, JR., JOHN G. TRUMP, and KENNETH A. WRIGHT, New York.

Observations on Epiphyseal Growth Potential Following Temporary Hypervitaminosis A. EDWIN G. BOVILL, JR., San Francisco.

The Substitution of Plaster of Paris Rods for Portions of the Diaphysis of the Radius in Dogs. LEONARD F. PELTIER and ROBERT LILLO, Minneapolis.

Healing of Fractures in Denervated Limbs. WILLIAM S. SMITH and E. R. DUNSFORD, Columbus.

The Determination of Callus Calcium in Healing Experimental Fractures Utilizing Radioactive Calcium. RICHARD T. ODELL, and J. ALBERT KEY, St. Louis.

Thursday, 9:00 a.m.–12:00 noon

CARDIOVASCULAR TOPICS, ACTH AND REPAIR

A New Prosthetic Replacement for the Aortic Valve. G. REHMI DENTON, PAUL FORMEL, and ROBERT LEATHER, Albany.

Total Cardiac By-Pass Utilizing an Intact Autogenous Lung for Oxygenation. MORLEY COHEN, RAYMOND C. READ, and C. WALTON LILLEHEI, Minneapolis.

Hepatic Hypothermia and Arterialization in Ischemic Shock Following Temporary Occlusion of the Thoracic Aorta. M. BEN, W. M. PARKINS, and H. M. VARS, Philadelphia.

Inhibition of the Stress Response During Surgery Under Hypothermia. WILLIAM F. BERNHARD and JAMES D. MCMURREY, Boston.

The Effect of ACTH and Histamine on Plasma Pepsinogen in Normal, Thyroidectomized, Hypophysectomized, and Adrenalectomized Dogs. K. KOWALEWSKI, H. A. HYDE, and S. T. NORVELL, JR., Edmonton.

The Effects of ACTH on Megakaryocyte Activity: Implications Concering Postoperative Thrombophilia. JOHN A. WILLIAMS, JOHN S. BELKO, and RICHARD WARREN, Boston.

Homologous and Heterologous Freeze-Dried Fascia Used to Repair Diaphragmatic and Abdominal Wall Defects. W. H. SEWELL and D. R. KOTH, Bethesda.

The Incidence of Fat Globulemia Following Soft Tissue and Orthopedic Operations. W. BRYANS and B. EISEMAN, Denver.

Endarterectomy and Replacement of Small Arteries with Special Consideration to the Surgical Therapy of Coronary Occlusive Disease. KAREL B. ABSOLON, JOSEPH B. AUST, and C. W. LILLEHEI, Minneapolis.

The Anatomical Results of Endarterectomy. WILEY F. BARKER, JACK A. CANNON, and LOUIS J. ZELDIS, Los Angeles.

INFECTIONS, CARDIOVASCULAR TOPICS

Respiratory Carrier Rates of Staphylococcus Aureus and Other Potential Pathogens in Surgical Personnel. JEROME J. LANDY, ROSS S. BENHAM, and ISABELLE HAVENS, Chicago.

Enhanced Antibody Production by Focal Radiation. JOHN B. GRAHAM and RUTH M. GRAHAM, Boston.

Treatment of Peritonitis with Tetracycline. CLEMENTE MOREL, Buenos Aires.

Pulmonary Hypertension with Increased Pulmonary Blood Flow. R. BEVERLY LYNN, DONALD M. HOSIER, and Henry T. BAHNSON, Baltimore.

Method of Myocardial Revascularization Using Internal Mammary Artery-Vein Fistulas. ORMAND C. JULIAN, H. C. COUTINHO, JOHN DAVIS, WILLIAM J. GROVE, and MAX S. SADOVE, Chicago.

Construction of Polyethylene Valves Based upon the Geometry of the Normal Aortic Valve of the Dog. JAMES F. BELL, ARTHUR S. HERMAN, RICHARD C. DEVER, and HENRY T. BAHNSON, Baltimore.

Experimentally Produced Pulmonary Valvular Stenosis. ANGELO RIBERI, PAUL GRICE, and WARREN COGGESHALL, Bloomington, Ind.

Experimental Replacement of the Aortic Arch and Descending Aorta with the Use of Permanent Shunts. WILLIAM E. NEVILLE and GEORGE H. A. CLOWES, JR., Cleveland.

The Use of Segmental Arterial Implants Prepared by Enzymatic Modification of Heterologous Blood Vessels. NORMAN ROSENBERG, E. R. L. GAUGHRAN, JOHN HENDERSON, G. H. LORD, and J. F. DOUGLAS, New Brunswick.

Physiologic Studies in Experimental High Output Cardiac Failure Produced by Aortic-Caval Fistula. DAVID C. SABISTON, JR., ERNEST O. THEILEN, and DONALD E. GREGG, Washington, D. C.

The Effects of Various Intravenous Infusions on the Survival of Burned Dogs. MORRIS J. FOGELMAN and BEN J. WILSON, Dallas.

Thursday, 1:30–3:00 p.m.

OBSTETRICS AND GYNECOLOGY

The Effects of Goitrogenic Drugs on Pregnancy and the Fetus. E. R. HUDSPETH and R. R. MARGULIS, Detroit.

Effects of Intravenous Pitocin Administration in the Development of Hypofibrinogenemia. ANDRÉ MARQUIS and R. R. MARGULIS, Detroit.

The Effects of Dietary Protein on the Metabolism of N^{15} Labelled Glycine in Pregnant Women. JOSEPH SEITCHIK and CARL ALPER, Philadelphia.

Cardiac Output in Pregnancy; Alterations During Labor and Delivery. EDWARD J. QUILLIGAN and CHARLES H. HENDRICKS, Cleveland.

Antagonism of Glucocorticoids and ACTH on Estradiol-17β Induced Uterine Growth. JOSEPH T. VELARDO and SOMERS H. STURGIS, Boston.

Peripheral Utilization of Glucose in Pregnancy—III, Insulin Tolerance. RICHARD L. BURT, Winston-Salem.

An Experimental and Clinical Re-evaluation of Chloroform Anesthesia in Obstetrics. PAUL R. BUERGER, GEORGE M. SANDERSON, JR., and ALBERT N. REKATE, Buffalo.

Carcinoma in Situ of the Uterine Cervix. LYNDON LEE, JR., P. J. MELNICK, and HARRY WALSH, Eloise, Mich.

Electrolyte Metabolic Balance Studies in the Postpartum Patient. ALLAN C. BARNES and JOHN BUCKINGHAM, Cleveland.

Hormone Metabolism in Pregnancy. E. JÜRGEN PLOTZ, Chicago.

The Evaluation of the Basal Cell in Radiosensitivity Studies of Carcinoma of the Cervix. ROBERT C. STEPTO, Chicago.

Friday, 9:00 a.m.–12:00 noon

NEUROSURGERY

The Choroid Plexus, a Potential Organ for Excretion. O. HUGH FULCHER, Washington, D. C.

Physiological and Therapeutic Effects of Bilateral Intermediate Midbrain Crusotomy for Atheto-Dystonia. RUSSELL MEYERS, Iowa City.

Clinical Results of Radio-Yttrium Hypophysectomy. ERIC T. YUHL, PAUL V. HARPER, DELBERT BERGENSTAL, and THEODORE B. RASMUSSEN, Chicago.

Studies in Cerebral Swelling. W. EUGENE STERN, Los Angeles.

Alterations in Cell Structure Following Sudden Increases in Intracranial Pressure. B. F. HADDAD, J. L. CHASON, J. E. WEBSTER, and E. S. GURDJIAN, Detroit.

Evidence of Reserve in the Parasympathetic and Somatic Innervation of the Urinary Bladder of Cats: a Preliminary Study Directed at Improving the Therapeutic Approach to Bladder Dysfunction in Man Following Cauda Equina Injury. A. Y. GEROL, J. W. ROBERTSON, D. CALLAN, and J. B. CAMPBELL, New York.

Vertebral Angiography by Retrograde Injection of the Brachial Artery. PURDUE L. GOULD, W. T. PEYTEN, and LYLE A. FRENCH, Minneapolis.

Electroencephalographic Responses in Dogs During Reduced Blood Flow. GUY OWENS, JOHN L. SAWYERS, and JAMES W. WARD, Nashville.

An Analysis of the Results of Treatment of Intracranial Aneurysm by Carotid Ligation. NICHOLAS WETZEL and RICHARD DAVIS, Chicago.

The Triceps Reflex. FRANK P. SMITH, Rochester, N. Y.

The Use of Plastic and Rubber Tubing in the Management of Irreparable Nerve Injuries. RICHARD WILLIAM GARRITY, San Diego.

Electroencephalographic Alterations Associated with Experimental Ventricular Fibrillation in Dogs. SANFORD E. LEEDS, EDWARD SHEV, and HAROLD ROSENBLUM, San Francisco.

FUTURE CLINICAL MEETINGS

1956—SAN FRANCISCO.....October 8 to 12
1957—ATLANTIC CITY.....October 14 to 18
1958—CHICAGO.....October 6 to 10